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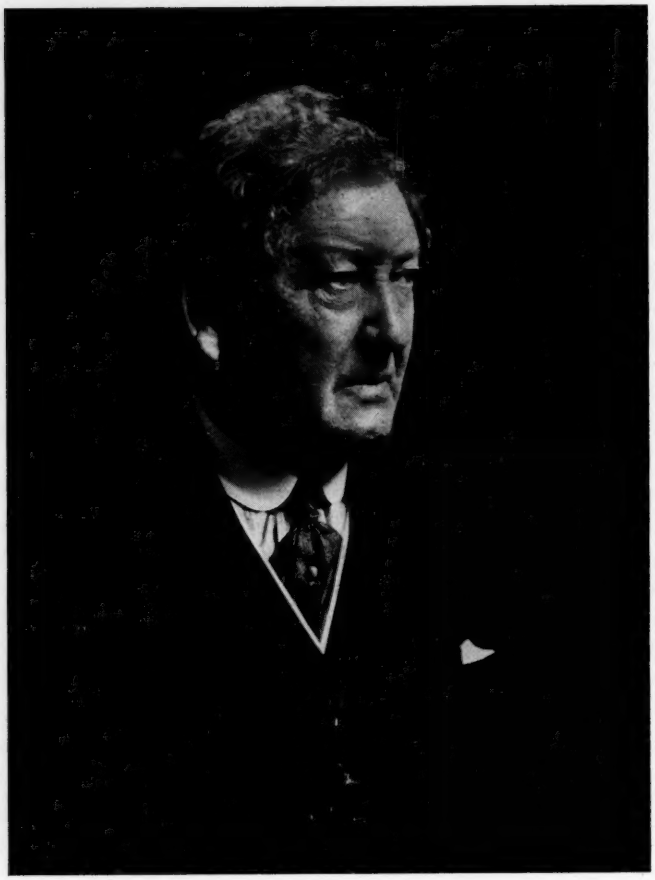
In Memoriam

SIR JOHN LYNN-THOMAS, C.B., C.M.G., K.B.E.

JOHN LYNN-THOMAS was born in 1861, the son of a Cardiganshire farmer. Forsaking farming, he became a student at the London Hospital, where he was House Surgeon and won the Hutchinson prize for an essay on Fractures of the Skull. After study in Vienna, he came to Cardiff in 1888 as House Surgeon to what is now the Cardiff Royal Infirmary. He took his F.R.C.S. (England), settled in Cardiff in 1892 as the town's first consulting surgeon, and in Cardiff he spent his professional life. He was successively from 1895 Assistant Surgeon and Surgeon to the Infirmary. He retired from practice and went to live in Cardiganshire in 1921. His time in Cardiff covered a period of great development of medical services in a rapidly growing city. Numerous consultants appeared, the staff of the Infirmary changed gradually from general practitioners to consultants, the Infirmary beds increased from 100 to over 400, and in 1921 it became the main teaching hospital of the new Welsh National School of Medicine. In all the rapid advances at the Infirmary Lynn-Thomas took a leading part. His original and inquiring mind was helped by many visits to surgical clinics on the Continent. In particular he was a great disciple of Theodore Kocher, whose work he much admired and followed.

Some of his most notable activities were: an excellent technique in facial reconstruction following extensive operations on mouth and jaws; his pioneer work in bone surgery; his invention, after the South African War, of a forceps-tourniquet by which main vessels such as the femoral were rapidly clamped through a small puncture; his skilful thyroid surgery, in which he was the first Cardiff surgeon to use local anæsthesia; his early abdominal surgery, resections and anastomoses; his original prostatectomy operation, a large curved forceps entering the prostatic bed from the suprapubic approach and made to project in the perineum, whence the enucleation was completed and where a special drain tube was inserted. These are just recollections. Lynn-Thomas's interests and work covered the whole surgical field and his publications were numerous.

Particular mention should be made of what was probably the first Cardiff removal of a cerebral tumour. This was a calcified intraventricular endothelioma showing well in the X-ray photograph. The patient was alive and well ten years later. The case is reported in full in the BRITISH JOURNAL OF SURGERY, 1921–22, 9, 490.



SIR JOHN LYNN-THOMAS. C.B., C.M.G., K.B.E.

1861—1939

Lynn-Thomas's private practice was large. In it he was somewhat erratic and very much a law to himself; he often went away for considerable periods. He started the first proper nursing home in Cardiff, a place of much use to him and his colleagues. While generous and kind if circumstances dictated, he was very insistent on his demanded fees, and this involved him in certain litigations. Once an action was brought against him and a practitioner, and his older colleagues will remember well the case of *Southern* v. *Lynn-Thomas and Skyrme*. A collection of £1800 was made from surgeons not only in this country but from all over the world to help to compensate him and his colleague for the expenses in which they had been involved, and Lucas-Championnière, then President of the International Surgical Society, presented the proceeds of the fund at a dinner in Cardiff.

To the Infirmary administration and welfare Lynn-Thomas gave much service. He presented the Infirmary with a large house adjacent to it, hitherto used as a nursing home, and also with a statue of Florence Nightingale. He took part in many public affairs, did much for the development of the Medical School, and was a prominent officer of the Red Cross.

Lynn-Thomas's war services were of great merit. He went with the Welsh Hospital to South Africa in 1900, and owing to the unfortunate loss of his senior colleagues, became its Commanding Officer. In the 1914–18 War he was much associated with Sir Robert Jones, became a Director of Military Orthopædics, and a Colonel in the Army Medical Service. He founded the Prince of Wales' Hospital for limbless soldiers at Cardiff, now an orthopædic hospital.

After retirement Lynn-Thomas interested himself in the Cardiganshire War Memorial Hospital and in archæological researches near his home.

Lynn-Thomas was made a C.B. in 1900, a C.M.G. in 1917, and a K.B.E. in 1919. He was an honorary F.A.C.S. and honorary L.S.A., and from 1919 to 1933 was a member of the Council of the Royal College of Surgeons. He served for a long period on the Editorial Committee of the BRITISH JOURNAL OF SURGERY. An original member of the Moynihan Chirurgical Club, he was much liked by his fellow-members.

No account of Lynn-Thomas would be complete without reference to his very distinctive personality. He was a big man with a great shock of hair. He was quite a character in dress, manners, and appearance. He retained his Welsh characteristics and was a regular 'Cardi'. He was unaffectedly egocentric, with marked likes and dislikes freely expressed. His appearance attracted attention wherever he went. Withal he was a kindly, likeable man, hospitable, pleased to see and entertain his friends, and endowed with a ready sense of humour.

Lynn-Thomas was a J.P., a D.L. of Cardiganshire, and its High Sheriff in 1907. He married in 1892 Miss Mary Rosena Jenkins, of Cardiff, who died in 1938. His only son died in 1928, and he leaves two daughters, one married.

MEDICAL PRACTICE AND MEDICAL EDUCATION
THE EXPERIMENTS OF THE MAYOS

WILLIAM JAMES MAYO, June 29, 1861 – July 28, 1939
CHARLES HORACE MAYO, July 19, 1865 – May 26, 1939

THE deaths of the brothers so close together in time made a single sad landmark in the history of surgery. Neither Doctor Will nor Doctor Charlie would have wished it otherwise, for together they had lived, together worked, and together planned.

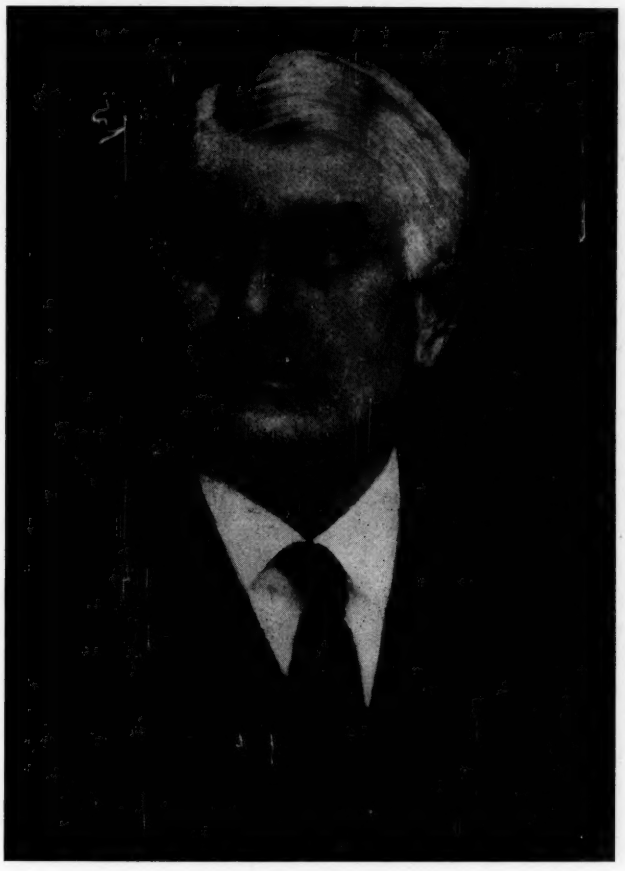
THE PREPARATION

They were sons of William Worrall Mayo, a native of Lancashire. After some training in physics and chemistry, their father emigrated to the United States at the age of twenty-six, and nine years later qualified as a doctor. Ultimately he settled in Minnesota, first at Le Sueur, where William James was born, and finally in Rochester, where he had gone in connexion with his work as a military surgeon, and where Charles Horace was born. Doctor W. W. Mayo was a practitioner of a type somewhat unusual at that time. He followed the progress of medicine, and to that end perfected himself in the use of the microscope; and he ventured with considerable success into the field of surgery. Moreover, he was always at pains to learn as much as he could from each case. The effect of such an environment on growing boys can best be stated in Dr. Will's own words: "My brother and I grew up to be physicians just as boys on a farm grow up to be farmers. We began by taking care of father's horses, keeping his office clean, and riding about the country with him on his calls. From the age of sixteen I was his first surgical assistant, and Charlie began giving anesthetic when he was a lad of twelve. Father performed as many post-mortem examinations as he could, and Charlie and I always attended. He had a good microscope, made in Germany, which cost $600, and I remember clearly that it was bought only after long discussion between father and mother, because the only way to get $600 all at once was to put a mortgage on our home." Dr. W. J. Mayo graduated M.D. in the University of Michigan in 1883, and joined his father in practice. Five years later Dr. C. H. Mayo graduated from Northwestern University; in the interval his older brother had built up a sound local reputation, and the two young men were able to relieve their father, who was now in his seventieth year, of the drudgery of the practice. The collaboration also made possible what had doubtless occurred to each—the founding of a surgical hospital.

THE FIRST EXPERIMENT

With the help of the Sisters of St. Francis, St. Mary's Hospital was founded in the autumn of 1889. It had fifty beds; five nursing sisters; a surgical assistant, Sister Mary Joseph, who was Dr. Will's assistant for many years; and the superior, Mother Alfred. Its medical and surgical staff was the Mayo family. St. Mary's

Hospital grew; in time additional hospitals were opened by a private corporation, until the available beds numbered between 1500 and 2000; this total was required to deal with the patients seen in the Clinic. The medical and surgical staff increased until there were more than 150 full-time practitioners on the permanent staff, and twice that number of young graduates undergoing instruction. There had been thirteen patients on the opening day of St. Mary's; recently more than a thousand patients registered at the Clinic in one day.

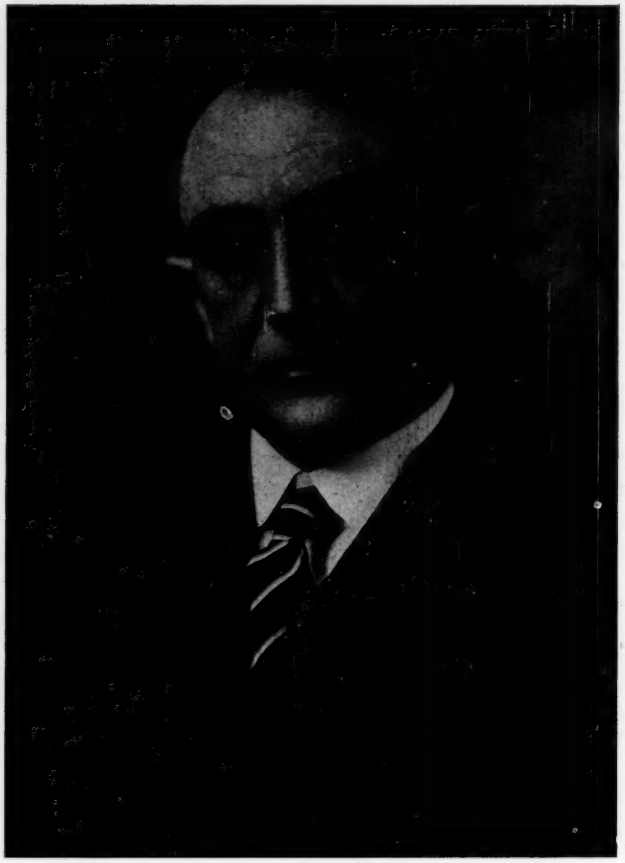


W. J. Mayo

The success of their first experiment was overwhelming; and as it provided large sums of money for the educational projects of the Mayos, some attempt must be made to analyse it. The brothers were courageous: the location of the hospital was almost a disadvantage, for Rochester was not a mushroom town, and its population remains at twenty-odd thousand; "Without the Mayo brothers," wrote an American newspaper, "the village of Rochester, Minnesota, would have been little beyond an entry in the Postal Guide." It was not on a main railway route, and until recent years the last stage of the journey to the Clinic was not more than tolerably comfortable; nor was it served by any great arterial road. The town

was not large enough to provide for its inhabitants, transient or permanent, such intellectual outlets as art, music, or the drama. Yet the patients came and continue to come, and the staff stayed and is happy.

The Mayos realized that, whatever the complaint, all the bodily systems must be examined, and that there must be available expert opinion on each system. At first they had to make themselves their own experts, but as the work grew they were able to train, or choose for assimilation, other physicians to ease these burdens;



and here it may be interpolated that both brothers were uncommonly shrewd and succeessful in choosing their colleagues. Naturally, as time went on, both the extent of the 'routine' examinations and the authority of the consultants grew. So sound had been the preliminary organization that the former continued to be overtaken smoothly. So steadfastly determined were the brothers that recourse to their plan should be financially possible to the poor as well as to the rich, that professional fees were never raised to a prohibitive level; indeed, though the practice was a private one, a goodly proportion of the patients did not pay fees, nor were fees required of them. Thus the basic principle of the work of the Clinic has been painstaking

complete investigation of its patients, if necessary by highly expert specialists, under one roof. The criticism has been made that the system is mechanical and soulless, without any close patient-doctor relationship. No more uninformed criticism could be imagined; for the Mayos were not only good organizers, they were very good doctors, and both by example and precept saw to it that this did not happen. Indeed, it was the writer's experience that consultants in the Clinic knew more of their patients' background than would those of similar standing in Britain.

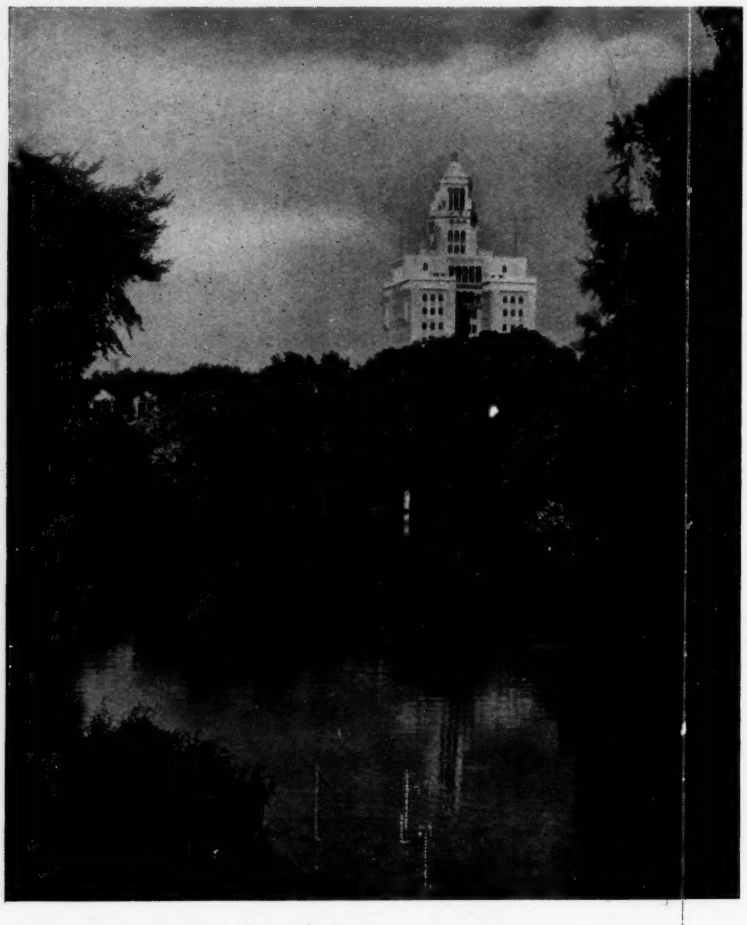
From their earliest days the Mayos had been imbued with two educational principles: the first was that they must travel widely to learn as much as possible from others; the second, that they would make it as easy as possible for others to learn from them. Their adherence to these principles has made it easy for their colleagues to add to their admiration respect and often affection. They were modest friendly visitors to other clinics. In their own institution, an important part of the organization is the maintenance of records on standard forms, so that they may be as full as possible; from the scrutiny of these the staff of the Mayo Clinic regularly shares its experience in monographs and papers. Visiting physicians and surgeons are made welcome, and may see the routine of diagnosis and treatment. It is almost literally true to say that for the last thirty years there has hardly been a day when the Mayo experiment was not being conducted openly before the eyes of the world.

THE SECOND EXPERIMENT

Probably Dr. Will had always had the dream of organizing post-graduate instruction to young America in clinical work and research. He chose as his instrument the University of Minnesota, and in 1913 the brothers offered to this body the total funds which had accumulated from their practice (an amount of over £300,000) to found the Mayo Foundation for Medical Education and Research. Incredible as it may seem, the State Legislature at first put difficulties in the way; but it was convinced by listening to an address by Dr. W. J. Mayo. Further sums have been added to the original gift, and the affiliation has been a success. Its genesis may be traced in the letter which accompanied the offer: "The fund which we had built up and which had grown far beyond our expectations had come from the sick, and we believe that it ought to return to the sick in the form of advanced medical education, which would develop better trained physicians, and to research to reduce the amount of sickness. My brother and I came to the conclusion that this purpose could be best accomplished through the state university."

Thus was launched the second Mayo experiment, and with wisdom and prescience the brothers included in the work of the Foundation not only clinical and preclinical subjects, but also such ancillary sciences as chemistry, physics, and experimental physiology. The experiment at once became, and has remained, a success. Young men and women were eager to avail themselves of the opportunities of the Clinic, and applications have always far outnumbered the posts available. Graduates have been welcomed from abroad, and other foundations have been given the courtesy of the Mayo Foundation. The stream of Mayo-trained physicians and surgeons has had a profound influence on American medicine and a considerable influence on medicine throughout the world: for those fortunate enough to have held a fellowship acquired not only methods of studying and treating patients; they acquired things more fundamental—the habit of simplicity in craftsmanship, the habit of honest appraisal of their own work, and high ideals.

Their second experiment successfully launched, the Mayos were in the heyday of their powers. Both were accomplished surgeons who had made important contributions to the technique of their craft. Both had an enormous clinical experience, which lent weight to their opinions, and enabled them to organize contemporary thought on many aspects of surgical therapeutics. Both were able organizers, and wise men of affairs in lay and professional matters. Both had been honoured by many learned bodies in the United States and abroad. Both had parts to play in



THE MAYO CLINIC

the direction of a large and successful institution, which had far-reaching responsibilities to medical endeavour. Both were helped in all their responsibilities by unswerving affectionate trust in each other, and by the happiest of family lives. Each was complementary to the other. Dr. W. J. Mayo thought first, farthest, and finally; his was the dominant figure. He kept himself somewhat apart from his colleagues, not from any lack of friendliness, but rather that he might continue to take a detached view of his projects, and so ensure impartiality in his decisions. One of his lifelong friends remarked that " when he put his shoulder to a wheel, it had to turn. Those who clung to the wheel might be flung off by centrifugal force; and if they clung

too long, they might be hurt." The warm personality of Dr. Charlie helped to weld the staff into a happy whole. His gaiety was as infectious as his wit was spontaneous and sparkling, and both were of incalculable value in creating and maintaining the spirit which permeated the Clinic. To ensure the success of their experiment they had at their command a picked staff. Their earliest lieutenants had been H. S. Plummer and E. S. Judd, who were to become famous in their own right; they were followed by a growing band of colleagues—often surprisingly young—imbued with the same enthusiastic ideals; and in H. J. Harwick they found an admirable head of their non-medical personnel. It is quite certain that the whole staff gave the brothers loyalty as well as expert service, and this was to influence, probably decisively, the third experiment conducted by the Mayos.

THE THIRD EXPERIMENT

As time passed, it was inevitable that there should be speculation about the future of the Clinic. The brothers were so outstanding, both professionally and personally, that many thought that its fortunes would begin to ebb when the Mayos began to participate less in its activities. This was certainly not the brothers' intention, and probably not their opinion, for in the words of the *New York Herald Tribune* " not even Hippocrates nor anyone else ever thought less about himself, or how impressive he was, and more about his hope of relieving suffering than did the pair." At any rate, they put the problem to experiment. Dr. Will announced that he was giving up operative work, and, quite characteristically, his reason for the step: " I observed younger men really possessed in the enthusiasm of youth the ability to grasp and orient new knowledge even though it conflicted with their experience—an ability I no longer had in so marked a degree." In due course Dr. Charlie did the same. The brothers had built truly, for the work of the Clinic continued to be scientifically and financially successful.

THE FOURTH EXPERIMENT

Although they no longer operated, both brothers continued to take an active part in the consulting work of the Clinic, and in its administration. The fourth and final experiment could not be of their own devising, although they naturally foresaw it, and had even been known to discuss it; for there remained to be tested the effect upon the Clinic when illness or death finally severed the brothers' connexion with the institution. The experiment was inevitable. Within the space of two months its two questions were posed, and triumphantly answered. Twice the Clinic paused to pay sorrowful homage to one who had been founder, leader, and friend. Twice, as the brothers would have wished, it took up again a full burden.

There is no surgeon who will not acknowledge a professional debt to these men. To those who had their acquaintance there will remain also the memory of their simple intensity, their uprightness, and their courtesy. Those they honoured with their friendship they bound to their ideals with unbreakable ties of affectionate loyalty. The medical historian of the future, seeking as he must to set down the biography of their minds, will see in their professional success the interest on the capital of their lifelong purpose—to bend science to the service of the sick.

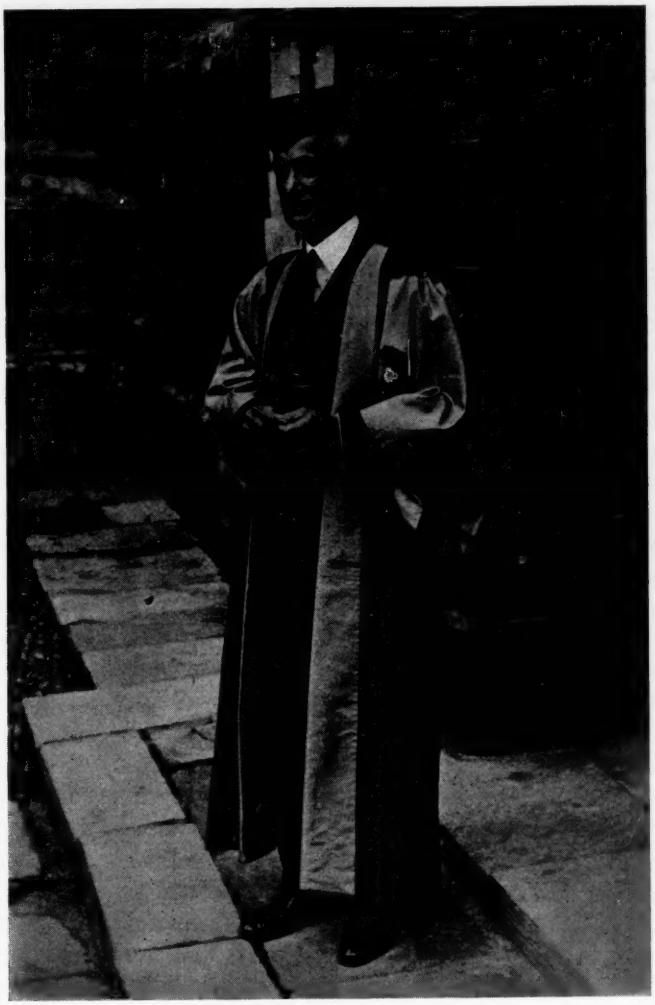
HARVEY CUSHING
(1869-1939)

FEW men in our profession have been so honoured as Harvey Cushing by the Universities and Learned Societies of the world; few have so excited the imaginations of their fellows; few have been so welcomed whether in public or private gatherings; and none have evoked more intimate friendships with such diverse personalities.

To relate, in the detail which it deserves, the story of his scientific pilgrimage would be too long a tale. When a man lives a long life it is the end rather than the beginning that is best known, yet the most useful lessons should be gleaned from the recollection of what a great man achieved in his twenties and thirties. It must suffice to say that his early work in the physiological laboratories of Kronecker, Kocher, and Sherrington taught him that there was a meaning for everything. He was the first to take frequent blood-pressure readings before, during, and after operations (he was probably the first surgeon to acquire a sphygmomanometer); his deductions all may read. Thus we find him, at an early age, watching his first neurosurgical cases post-operatively as if they were important experiments, not content to believe that an unexpected alteration was but the natural result of an unnatural procedure. Rather was it likely to be the work of some visible agent which could be undone by bold measures, even by the re-opening of a wound scarce sewn up. For Harvey Cushing was, above all, courageous. Thoughts of what the residents or his colleagues would say if he did something unconventional never entered his head, or, if they did, they disturbed him not at all.

The influence of Halsted upon him was enormous, but it was a bilateral affair, for many of the master's principles are better illustrated by the pupil's work. Nor was it Halsted alone who set the seal of Johns Hopkins upon him. He found it in the first flush of its glory with the original great holders of the Chairs—Osler, Halsted, Welch, and Howard Kelly—nearing, rather than past, the height of their powers. A glance at the contents of the famous *Bulletins* of those years gives an impression of imagination, of power, of drive, which could scarcely be surpassed. He was fortunate in being transplanted at an impressionable age into those surroundings. And there, too, was the Historical Club, from which he derived so much and to which he gave back, vicariously, so freely. Osler, especially, recognized his qualities, and how that friendship developed is well known. An idea of the exceptional capabilities of the young Harvey Cushing can be obtained from his description of the work of the Hunterian Laboratory at Baltimore, of which Halsted had made him the Surgical Director. In his paper of 1906 he made a clear-sighted analysis of the relationship of Surgery to the parent body of General Medicine, and gave an outline of an ingenious method of teaching the subject which he called " Operative Medicine ". He remained especially proud of this work to the end of his days. That title is important because Harvey Cushing was a first-rate doctor, holding that " only in the dosage, as it were, in which they administered operative therapy are physicians and surgeons apart ".

Most men are satisfied when a diagnosis has been made and a decision reached as to the line of therapy. Cushing was never content with that alone; the case would be then but half complete, and the best still to come. It was this—what piece of knowledge could yet be wrung from the clinical state, in what way did it illustrate some principle of normal or abnormal physiology or anatomy, and if there was some loose



HARVEY CUSHING
1869—1939

end that did not quite fit with the general facts, where did it belong and what did it mean? It was in this that he was the nonpareil. Trained to animal experiment, he was ready to solve by that means such problems as could find answer no other way, but if possible it should come from clinical study. Each of his cases must be made to teach him something; let each, therefore, be scrutinized, however familiar the facts might seem to be, lest some features were different. Every patient must be followed

up, each made to feel that here was someone deeply interested in his welfare, someone to whom he would instinctively turn if things again went wrong. In this way he got the information for reviews of the life history of tumours which often called for a revision of cytological structure and eventual qualification of the original laboratory conception. His disentanglement of the varieties of cerebellar tumour was a master's work; and although he pointed out the variations in symptomatology that ensue upon different tumour types, he never ventured far into neurophysiological speculations—indeed, he always disclaimed any profound knowledge of neurology. It is interesting, for example, to observe that he wrote next to nothing on epilepsy, even in his younger days, when what we now know to be mistaken claims for its common surgical curability were table-talk. One concludes that he knew with uncanny instinct where the richest ore lay beneath the yet scarcely broken ground. He held that tumour work was the cream of neurosurgery, and that though one might, when half-fledged, have to busy oneself with traumatic work or hydrocephalus or epilepsy, it would be well not to let these difficult subjects become masters when there was so much to do elsewhere. So it befell that only in his visual-field work, which gave such important practical results, did he go deeply into neuro-anatomical analysis.

As a clinician he was more than competent; he never let a mistake go by without the fullest, and even wearisome, inquiry into its reasons. He would tolerate no glossing over of failures, and indeed it is remarkable that a man who was so much the creative artist, that a man who saw such visions, should not have fallen deep into the trap of forcing his facts to prove his points. From his earliest days he made a practice of publishing his operative mortality. He did this first because it was necessary for him to prove to an incredulous world that neuro-surgery was not beset with a depressing and terrifying mortality, but he did it, too, because of his deep faith that he could continuously better his performance. He was almost frightening in his belief that whatever the lesion was (unless hopelessly malignant) he could always show vastly better results in the next five-year period, frightening because such confidence seemed to invoke the wrath of the gods. Yet time proved that he was right, and no one to-day questions the accuracy of his figures, though there always were, and always will be, men of small stature or sour minds to whisper behind hands at the doings of their betters. He was a slow operator, but this was the Halsted tradition; his nature originally inclined rather to the ultra-speedy school of Boston in which he had been trained (though that city does not deserve to be so singled out as the prototype of a then almost universal creed). He could take no risks because there was so much to discover, but in his latest years he became much quicker, for he had learned what he wanted. It is the disaster of our short lives that we spend nearly all of them in acquiring knowledge that is difficult to impart; youth must tread the same path almost from the beginning. The sick recognized that he understood them, sympathized with them, would protect them in every way possible against disaster, and if at times he undertook to operate upon them " with some misgivings " (a favourite phrase of his), they knew intuitively that he would, so far as could be, follow his principle " in case one can accomplish nothing, the next most desirable thing is to do no harm ". He was next greatest in his relationship to his pupils and his friends. His vivid personality, his controlled dæmon, his intellectual fire, inspired them all; he drove them unmercifully, but purposefully, and often almost to the point of rebellion, when he would, by his own

particular brand of magic, charm them back again. He would become the tender, humorous companion whom we all loved. His output was enormous when one considers how much time he spent in the operating room. He wrote 13 books and 330 papers and addresses, but almost more significant is the fact that his assistants, whilst in his service, wrote 328. He himself wrote vividly, but with that difficulty common to the more practised authors. He wrote and revised and wrote again, and always in his works are sly references to the great of other ages, little twists of phrases that give his work its attraction. Though his constructions might at times outrage the pedant, the great thing was that he had something vital to tell, some new instalment of the mystery story of disease to give, some glimpse of a new nosological or therapeutic possibility to disclose, that came the better from his own distinctive manner.

He was moody, but he disciplined himself severely and would not let his mind waste itself in frivolities; for that reason he was bored by casual conversation. But what a fascinating story teller he could be; his contemporaries he never discussed; if he thought they did well, he would say so and pass on; if they did ill, he made little comment. He realized that the man who worried over much about what other people say or do, or even what other people want, distracts himself and diminishes his own powers. So strong a personality must necessarily call forth antagonisms. He had a great conception of the surgeon's duty and of that of holders of professorial chairs. In the best schools the latter should be safeguarded from grubbing after dollars in that most satisfactory of all ways, the conditions of their office, but they fulfilled their highest destiny not in lecturing well or often, not in the pure organization of teaching, but by the distinction of their intellectual attitude towards their work, by the continuity and integrity of their endeavour to add to knowledge, in the training of their assistants in technical methods, more especially in ways of thought. In conversation he once made this pregnant remark: " I should like to see elected as Professor of Surgery a man who had no hands "! As Moseley Professor of Surgery at Harvard (1912–1932) he exhibited these qualities to the full; without the powers with which that office invested him he could not have accomplished so much. But he was clearly born for high place.

In his closing years at Yale, as Sterling Professor of Neurology and Director of Studies in the History of Medicine, he was able once more to visit (as he was wont to do) the scenes of his youth, to cast aside his years with those somewhat nostalgic searchings of memory which are the privilege of age, to recall his feats in the baseball team, to see Yale again in moonlight, to hear from the shadows below the notes of a piano from a lighted window.

It was with thoughts of the surgical philosophy which he had evolved, and with a mental picture of his disciples gathered around him, that on his seventieth birthday Wren's epitaph, " Si monumentum requiris, circumspice ", was sent to him. This JOURNAL did him the honour of dedicating its May number to him, and now these few months later we must needs mourn him. But let us also give thanks for the marvels that he achieved, and bid him farewell with the words of Sir Thomas Browne, willing that his " bones lie soft, and the earth be light upon them ".

AN UNUSUAL CASE OF OBSTRUCTION TO THE COMMON BILE-DUCT (CHOLEDOCHOCELE ?)

By SIR W. I. de COURCY WHEELER

In December, 1915, a note was published[1] of a case of biliary obstruction, in which at the time there was no satisfactory explanation to account for the conditions found at operation.

The patient was a doctor aged 65 years. He stated that he had been operated upon elsewhere for repeated attacks of biliary colic and jaundice. The abdomen had been opened by a long vertical incision with transverse extension which resulted in a large ventral hernia. On this occasion the common bile-duct was found dilated, but no stone or other cause of obstruction was revealed.

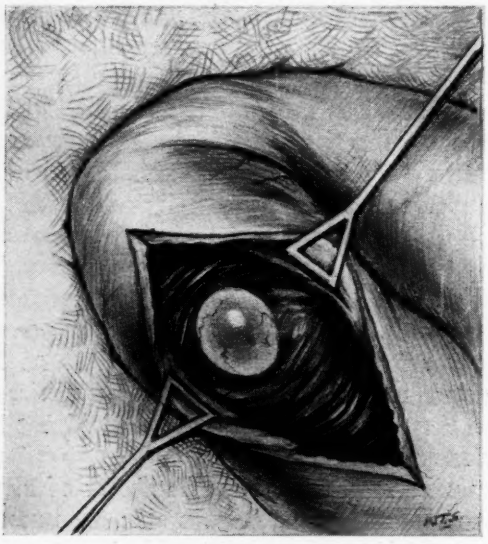


Fig. 328.—Appearance of cyst in the region of the orifice of the common bile-duct when the duodenum was opened.

The symptoms continued. The abdomen was reopened (July, 1910). The gall-bladder could not be found amongst dense adhesions, and may have been removed at the previous operation.

The common duct was exposed and was seen to be greatly dilated. No stone could be felt. The pancreas and duodenum appeared normal.

The duodenum was opened and the cause of obstruction at once became apparent. A small tense cyst, about the size of a cherry, occupied a position in or about the orifice of the common duct (*Fig.* 328). The cyst was incised, and the field of operation immediately became flooded with bile.

The patient was kept under observation for five years. He had no recurrence of pain or jaundice, and died subsequently of some medical ailment, when approaching eighty years of age.

The case was mentioned to the late Lord Moynihan, and more recently to the late Sir David Wilkie. No similar condition had been observed by them.

Recent experiences in a hospital for genito-urinary diseases recalled this case to mind, and suggested the possibility that the common bile-duct could become obstructed by a mechanism similar to that seen in the ureter in the presence of ureterocele. Cystoscopic examination in cases of ureterocele revealed a picture

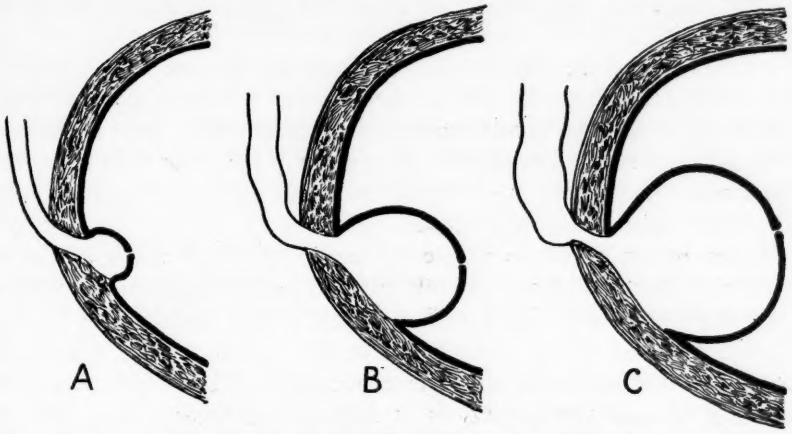


FIG. 329.—Progressive stages in the formation of ureterocele. A, B, and C show the loosening up of the vesical mucous membrane and the production of hydro-ureter from back-pressure. (*Atfer Gutierrez.*)

very similar in appearance to the cyst seen when the duodenum was opened, and it occurred to the writer that the aetiology might be the same.

Various authorities refer to ureteroceles as forming cysts ranging from the size of a hazel-nut to that of an orange, and occasionally, in the case of infants, filling the entire bladder. If small, a ureterocele may be harmless and go undetected.

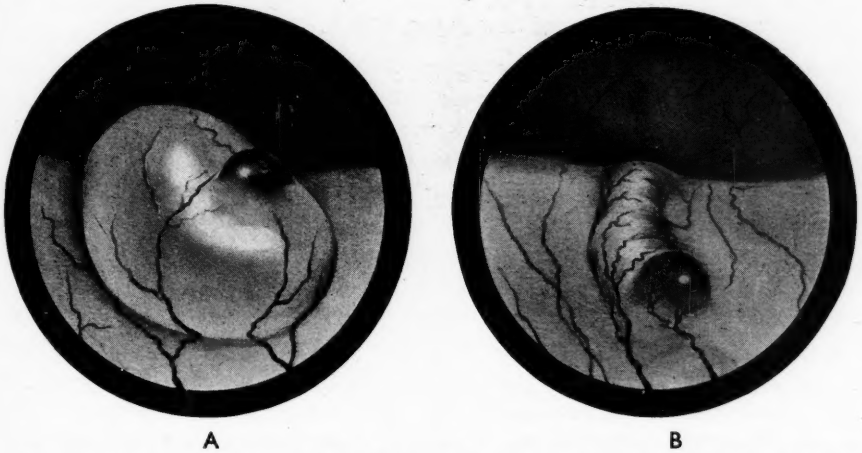


FIG. 330.—A, Ureterocele distended with urine; B, Ureterocele collapsed by discharge of urine. (*From Canny Ryall's 'Operative Cystoscopy'.*)

It may, on the other hand, be squeezed against the orifice of the ureter and cause obstruction during contractions of the bladder. Gutierrez[2] states that "This hydraulic and cystic dilatation of the intravesical portion of the ureter is in many cases the result of a congenital malformation or obstruction at the ureteral orifice, which sooner or later will produce a definite interference with the proper drainage

of the kidney and ureter" (*Fig.* 329). Pain and bladder tenesmus are frequent symptoms; hydro-ureter and hydronephrosis are end-results.

Assuming that an analogous condition may cause obstruction to the common bile-duct, as the case under review appears to suggest, persistence of pain and jaundice after operation may not be so often the result of an elusive stone as the literature proclaims.

Cystic dilatation of the intraduodenal portion of the common bile-duct would be difficult to detect. A sound passed through the common duct for exploration would appear to enter the duodenum without hindrance. In an early case the dilatation would only be evident during the passage of bile, just as in the case of early ureterocele which only is seen immediately before or during the ejaculation of urine (*Fig.* 330). Late cases are fixed and permanent.

The theory that a condition similar to ureterocele may occur at the orifice of the common bile-duct, based on only one case, is put forward with diffidence, more especially as the literature is silent on the subject. One definite fact is established. In all obscure cases of biliary obstruction in the presence of a dilated bile-duct, search should not be abandoned until the duodenum has been opened and explored. The cystoscope reveals ureterocele as it fills and empties; only late and fixed cases of choledochocele would be detected at the orifice of the common bile-duct during trans-duodenal exploration.

Mr. Shields kindly made the drawings (*Figs.* 328, 329, and 330) to illustrate the conditions referred to above.

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[2] GUTIERREZ, *Surg. Gynecol. and Obst.*, 1939, March.

SENSIBILITY IN THE ABDOMEN

By VICTOR J. KINSELLA, Sydney

Two hundred years ago physicians had no difficulty in understanding abdominal pain. Thomas Willis dissected and Christopher Wren illustrated the great visceral nerve-plexuses. It was clear to Willis that these subserved the motor and sensory functions of the viscera. He stated that the viscera and their nerves do not disturb consciousness unless gravely disordered, but that they are endowed with an "exquisite sensibility as well as a motor faculty" which is brought into play in disease, warning the organism and helping it to expel the disease. There was the viscus, and there was its direct nervous pathway to the sensorium, for use when needed.[1]

But this simple position was disturbed about forty years ago by the observation that the viscera can be painlessly cut, burnt, and stitched. Moreover, it came to be believed that not only were the healthy viscera painless, but also the viscera in disease. Elaborate hypotheses were formulated to provide indirect pain pathways from the viscus to the sensorium. But clinical evidence of direct visceral sensibility was still strong. Osler wrote "the gall-bladder may become palpable and very tender". Friendly scorn was poured by Mackenzie on such statements, and he accused observers of forgetting that the sensitive body wall intervened between the viscus and the hand of the examiner. Hurst and others compromised, admitting the possibility of spontaneous visceral pain, but denying the possibility of induced visceral pain (tenderness).[2]

In an attempt to shed light upon these difficulties, 40 cases of appendicitis were operated upon under local anæsthesia and observations made of the sensitivity of various parts. Most of these operations were carried out at St. Vincent's Hospital; some at Hornsby Hospital.

The dose of morphia given to the earlier cases was $\frac{1}{6}$ gr. and $\frac{1}{4}$ gr. The later cases received either no premedication, or 30 gr. of potassium bromide and 10 gr. of chloral hydrate and no morphia. In many of the acute cases this was vomited and in others probably not absorbed. Novocain was used as the anæsthetic agent, in $\frac{1}{2}$ per cent solution with adrenaline 1–300,000.

A skin wheal with a hypodermic needle was made about 1 in. above the right anterior superior iliac spine. The skin was then infiltrated, keeping close to the dermis, by a long needle passed medially through the wheal. In those cases where Lemaire's work was being repeated this infiltration was made over a very wide area, medially almost to the middle line, inferiorly almost to the inguinal ligament, and superiorly towards a point just above the umbilicus. About 50–60 c.c. of $\frac{1}{2}$ per cent novocain was used in these cases. Next, the needle was passed through the external oblique and a deep muscular infiltration made. Medially it was passed as far as the lateral border of the rectus, and could often be felt to pierce the lateral margin of the rectus sheath. The needle was then passed posteriorly, and a deep muscular infiltration made in the flank in the hopes of blocking the twelfth thoracic, ilio-hypogastric, and ilio-inguinal nerves. This last step was abandoned soon after

the investigations upon the posterior parietal peritoneum were commenced. The abdomen was opened by McBurney's gridiron incision.

Of these 40 cases, 22 were acute, with well-marked clinical tenderness, and 18 were 'interval' cases with little or no clinical tenderness.

In many cases it was not possible to carry out a complete set of observations, in some on account of technical difficulties, e.g., in delivering the appendix, and in others on account of the general stress and discomfort of the operation.

The operation notes of 3 cases are given in detail in order to illustrate the method of investigation. The observations made in the 40 cases are then grouped and reviewed in subsequent sections.

Case 12.—Mr. W., aged 30, Hornsby Hospital, September 27, 1937. Bromide was vomited. The patient was admitted with a diagnosis of intestinal obstruction. In the ward the pain was umbilical, severe, and colicky. The house surgeon confirmed the diagnosis of acute intestinal obstruction. The severe pain continued on the operating table and was practically continuous. Tenderness was present, but only when the thick palpable appendix could be pinned down and rolled under the finger. Injection of the parietes did not affect the pain and tenderness. Squeezing the appendix caused definite aggravation of the umbilical pain; squeezing the cæcum had no effect. The mesentery was then injected, and the umbilical pain ceased in dramatic fashion and a complaining patient needing continuous admonition and encouragement became quiet and comfortable during the removal of the appendix and the closure of the abdomen. The appendix was very tense, red on the surface with a darkening point of pre-gangrene, tensely distended behind a fibrous stricture at the base.

Case 13.—Miss A. M., aged 27, Hornsby Hospital, September 28, 1937. No premedication. Continuous griping umbilical pain. Slight tenderness in the right iliac fossa, causing pain to radiate to the umbilicus. After injecting the abdominal wall, tenderness became less marked. The appendix was thick and red, mucosa grossly thickened and red, with a large fæcolith in the dilated distal part, the base narrower and less affected. Umbilical pain was markedly aggravated on squeezing the appendix, causing the patient to writhe. Cæcum painless. The mesentery was injected, the umbilical pain ceased, and the rest of the operation was painless.

Case 19.—Mr. G. O., aged 30, St. Vincent's Hospital, October 25, 1938. Bromide and chloral. Tenderness present. Infiltration just beneath skin (using 50 c.c. of novocain solution) diminished, but did not abolish, the tenderness. The anæsthesia was tested by drawing the point of the knife over the skin, and found to be effective over the tender area. The posterior parietal peritoneum was slightly tender to stroking, more tender to picking up with forceps, and to spirits. Pain was referred to umbilical area. The appendix was very long and thickened, and acutely inflamed, with fibrin on it. It had been obstructed and distended, but the contents had emptied themselves into the cæcum. The lumen was grossly distended and the wall thinned behind a sharply marked ring of pre-gangrene. The appendix was easily withdrawn from the abdomen and allowed to rest, untouched, in its whole length on the skin towels. The patient had no pain. The appendix was squeezed firmly by the thumb of each hand on the one side, and the index and middle finger of each hand on the other side. The patient grimaced and complained of pain referred to the centre of the abdomen. This was repeated with similar effect. The pain appeared to persist after the squeeze had been relaxed and only gradually disappeared. An artery forceps was now opened and the blades placed on each side of the mesentery and left open. The mesentery was then cut across in its whole width by one snip of the scissors. The patient grimaced and complained of pain in the centre of the abdomen. The artery forceps was then closed on the mesentery; the patient winced and stirred and complained of severe pain in the centre of the abdomen until the mesentery was infiltrated with novocain, proximal to the forceps. Traction was avoided.

The tip of a curved hæmostat was now passed along the anterior parietal peritoneum up towards the right costal margin. This caused pain "up towards the ribs on the right side".

OBSERVATIONS ON PARIETAL ANÆSTHESIA

One of the most interesting of recent observations upon abdominal pain is that the pain and its associated phenomena may be profoundly modified by local anæsthesia of the abdominal wall, either in its full thickness or in the skin alone. Perhaps this should not surprise us, because for generations the patient has modified his abdominal pain by a hot or cold application, or by rubbing in some favourite extract of herbs and simples. It is well worth calling to mind the observations of John Hilton on this point, in his *Lectures on Rest and Pain.*

In 1926 A. Lemaire[3] published observations in which novovain (12 cases) and freezing (5 cases) had been found to modify abdominal pain. He finds in most cases that the pain, tenderness, and rigidity disappear on anæsthetization of the abdominal wall. In one case of biliary colic he noted complete failure to modify the attack, and in a case of tumour of the lesser curvature he noted no effect by skin infiltration, but a marked diminution after full-thickness infiltration.

In 1928 S. Weiss and O. Davis[4] described their experience in 25 cases. They anæsthetized the skin only, and stressed the importance of injecting the novocain as close to the dermis as possible. They did not concern themselves about the tenderness and rigidity, but found complete relief of the pain in 21 cases, relief in 3, and no relief in 1.

In 1929 J. Morley[5] investigated 11 patients. Out of 10 cases the spontaneous pain disappeared or diminished in 8, moved in 1, and was not affected in 1. Out of 11 cases the deep tenderness was diminished in 4, doubtfully diminished in 2, and not affected in 5. Out of 5 cases the rigidity remained unaffected in 4. Note the difference in effects upon the spontaneous pain, the tenderness, and the rigidity. This difference is also obvious when the cases of other observers are studied. It may be pertinent to ask why this difference should occur if the lateral pain, the tenderness, and the rigidity depend upon the same peritoneoparietal reflex. Perhaps there are other factors—for example, visceroparietal reflexes and psychic influences.

In 1930 R. D. Rudolf and A. G. Smith[6] confirmed these observations. They found that in some cases the superficial pain was lessened but a deep sense of discomfort remained; in several, both superficial and deep pain disappeared. Where no definite superficial pain was present, but only deep suffering, as in intestinal colic, no relief was obtained.

In 1932 H. H. Woollard, J. E. H. Roberts, and E. A. Carmichael[7] made observations upon the shoulder-tip in 9 cases in which they stimulated the phrenic nerve during the operation of phrenic evulsion. In no case was the referred pain affected by infiltrating the area of referred pain with novocain.

In my own cases spontaneous pain was investigated in 5 instances. Skin infiltration caused a diminution in 2 of these, and the subsequent muscular infiltration caused its disappearance in one case and further diminution in the other. It disappeared after full-thickness infiltration in a third case. In two others it had no effect.

Deep tenderness was investigated in 21 cases. Skin infiltration caused a diminution in 5 cases and no effect in 10. The subsequent muscular infiltration caused a disappearance in 1 case, a further diminution in 2, and no effect in 8. A full-thickness injection caused a disappearance in 3, diminution in 1, and no effect in 2 cases.

These last two cases are remarkable, because the tenderness was extreme, and quite unaffected by the cutaneous infiltration. Both the patients were of inferior mental type, manifested extreme nervousness and fear, unreasoning and beyond control by psycho-anæsthesia. It appeared that the parietal injection was of little effect, because the psychic element predominated.

REVIEW OF OBSERVATIONS ON THE ANTERIOR PARIETAL PERITONEUM

The anterior parietal peritoneum was stimulated in 18 cases by passing a curved hæmostat through the wound so that its point stroked along the inner surface of the abdominal wall. This had no effect until the point had passed well away from the area of operation. But as the forceps approached the unanæsthetized right costal margin, or the middle line, the patient invariably (in all 18 cases), complained of pain. It is not uncommon when the wound is being closed to find that the passage of the needle through the anterior parietal peritoneum causes a painful response, although the patient remains unconcerned during the suture of the other layers.

Localization was studied in 11 of these cases. In 1 case the pain was definitely and persistently referred to the middle of the abdomen. In 1 case, suturing the peritoneum caused a middle line pain, although stroking with a curved hæmostat caused a well-localized right-sided pain. In 9 other cases the pain was well localized (" up towards the ribs, on the right side ", etc.). In 1 case the patient could not tell the whereabouts of the pain.

These observations confirm the conclusions of Lennander, that the anterior parietal peritoneum is a sensitive layer, which seems to be like the cornea, and appreciates only pain sensation and in most cases localizes the stimulus with accuracy.

REVIEW OF OBSERVATIONS ON THE POSTERIOR PARIETAL PERITONEUM

Although the anterior parietal peritoneum has been thoroughly investigated by Lennander and by Morley, the importance of the posterior parietal peritoneum has been overlooked. Lennander described 3 cases in which he introduced a finger and an instrument between the intestinal coils and pressed firmly upon the parietal peritoneum in front of the vertebral column. This crude stimulus produced inconsistent results. Morley,[8] on hypothetical grounds, actually rules out the posterior parietal peritoneum as a factor in abdominal tenderness. He supposes that this layer is supplied by lumbar spinal segments and that if it were responsible for pain, the pain would be referred to the lumbar dermatomes. He is here discussing peptic ulcers, and he makes it quite clear that it is the anterior parietal peritoneum which is the important layer. Later, he attributes the right-sided pain of an acute appendicitis to irritation of the anterior parietal peritoneum. But it should be noted that the appendix springs from the posterior aspect of the cæcum, lies in contact with the posterior parietal peritoneum, is only rarely a contact relation of the anterior parietal peritoneum, and is usually separated from this latter layer by cæcum, coils of small intestine, and perhaps omentum. So the anterior parietal peritoneum can only be of late importance in most cases of acute appendicitis, when the inflammatory exudate is free enough to pass between coils

of bowel and reach the anterior abdominal wall. But many cases of acute appendicitis with pain in the right iliac fossa show no inflammatory exudate at operation. In 49 of a series of 50 consecutive acute cases with pain in the right iliac fossa operated upon by the author, there was no contact of the appendix with the anterior parietal peritoneum, and in 30 of these 49 cases there was no free fluid. But all these 30 appendices were in contact with the posterior parietal peritoneum. It seems clear, therefore, that the sensibility of this layer should be investigated.

To my surprise the first four cases showed absolutely no sensitivity in this layer. I reconsidered my technique. The patients had not had morphia and they responded well to other stimuli. I abandoned the injection given posteriorly into the muscles of the loin. I carefully swabbed away excess of novocain from the wound before dividing the serous layer. I packed away the cæcum medially and upwards with ribbon gauze well rung out with saline, and able to absorb any novocain squeezed out of the wound. The posterior parietal peritoneum, below the area of fusion of the embryonic mesentery, then came into view, very often as far medially as the iliac vessels. It was stroked with the tip of a curved artery forceps, grasped with the forceps and pulled into a small tent, touched with a tiny piece of gauze soaked in alcohol; and in a few cases pressed with a finger-tip against the psoas muscle.

Of 20 patients who were investigated, 10 showed absolutely no response; 1 showed no response from the first two pinches with the forceps but from the third she felt a very slight pain; 9 showed pain varying in degree from slight to marked.

The bearing of these observations on the clinical difficulty of the retrocæcal appendix needs no stressing.

The site of pain reference was investigated in 9 cases. It was referred in 5 cases to the right iliac fossa; in 1 to "the right hip bone"; in 1 to the right side passing through to the back; in 1 the pain was first localized to the centre of the abdomen and later stimuli to the right iliac fossa; in 1 the pain was referred emphatically on repeated stimulations to the centre of the abdomen.

OBSERVATIONS ON THE SENSITIVITY OF THE MESENTERY

My method of dealing with the mesentery is to pass a silk ligature through it close to the appendix, tie the ligature, then cut the mesentery. If the ligature carrier is gently pressed against an avascular spot and its point cut down upon by repeated little touches with the scalpel it can be slid through the mesentery without pain. The mesentery is insensitive in its avascular areas. The least jerk (or tearing) will cause pain.

In the first case in which the operation was completed under local anæsthesia (*Case* 3), tying of the ligature caused such severe epigastric pain that I anæsthetized the mesentery in the next four cases before ligating it. In *Cases* 7 and 10 I gently squeezed the mesenteric edge, containing the vessels, and the painful response confirmed my respect for its sensitivity and I continued to anæsthetize it before ligation. However, after reading Lennander's conclusion, that the mesentery is insensitive, I continued my investigations. The stimuli applied were a light squeeze, a heavy squeeze and crushing with artery forceps, ligaturing, cutting through with scissors and with thermocautery. The mesentery was investigated in 20 cases;

in every case pain resulted from the stimuli enumerated, and in most cases the pain was severe. In one case, placing an artery forceps on the mesentery caused no pain, but when it was removed and a ligature tightened in the groove which had been made, marked pain resulted. Perhaps the microscopic nerve-fibres could find sanctuary in the grooves of the forceps blades, but could not escape the grip of the silk ligature. The explanation of the difference between my results and Lennander's will be given later.

In all these cases the greatest care was taken to avoid pulling upon the parietal attachments of the mesentery.

Tying the silk ligature causes the most intense pain, clamping a pain of less intensity, and cutting through with scissors or the thermocautery the least intense pain.

In one case holding the cautery near the mesenteric edge so that the latter became hot caused pain. In another case a light quick touch with the cautery on the mesenteric edge, which destroyed the endothelial layer but could not have heated deeply, caused no pain.

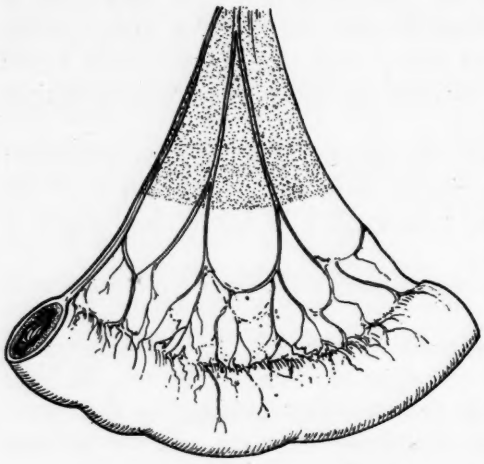

FIG. 331.—Diagram of the nerve-supply of a segment of the alimentary canal with mesentery. The sensitive parts correspond with the nerve-fibres. The shaded area at the root of the mesentery is, according to Morley, sensitive; the rest insensitive. This latter conception is unphysiological.

It seems, then, that the mesentery taken as a whole is very sensitive to mechanical stimuli, that its endothelial covering and avascular areas are insensitive, and that the sensitivity resides in the nerve-fibres which mostly follow the vessels (a few free nerve-endings and an occasional Pacinian corpuscle may be found histologically in the avascular spaces). *Fig.* 331 contrasts these findings with Professor Morley's unphysiological conception of an abrupt demarcation between a sensitive area at the root of the mesentery and a non-sensitive area adjoining the intestine.

In 16 cases the site of reference of the pain was noted. In only 1 case was it referred to the right iliac fossa; in the other 15 it was median (umbilical in 11, epigastric in 2, all over the abdomen in 1, "shooting up from the middle of the stomach" in 1).

REVIEW OF OBSERVATIONS ON THE SENSITIVITY TO SQUEEZING OF THE ACUTELY INFLAMED APPENDIX

When studying the sensibility of the viscera it is important to bear in mind: (1) That their nerve-supply is sparse (Langley pointed out years ago that the total number of afferent nerve-fibres supplied to the whole of the viscera of the cat is about the same as the number in a single posterior spinal root); (2) That the nerve-fibres destined for the viscera and their nerve-cells are much smaller than the somatic nerve-fibres and cells; (3) That the individual afferent neurones in the viscera are probably less efficient from the sensory point of view and more akin

to the primitive sluggish nerve network than are their fellows of the body wall, which have become specialized to keep close watch on the environment.

Thus, a stimulus does not disturb consciousness unless it is a massive one, and our viscera work and move smoothly and silently. If the healthy appendix is cut, or crushed by artery forceps, no pain results because few fibres are stimulated. But if the vascular margin of the mesentery is cut through with scissors, or clasped with forceps, pain results because numerous fibres are stimulated. In painful visceral disease a massive area is concerned and not just a restricted area as would be affected by cutting. In appendicitis the whole or most of the organ is affected. In the case of colic large tissue masses are affected; for example, in labour pains the body of the uterus can be felt to harden; the pains produced by a barium enema under too high pressure can be seen under the fluoroscopic screen to synchronize with powerful contractions of large segments of the colon. In visceral disease, I believe that pressure upon the nerve elements, just as in somatic disease, is a natural adequate stimulus.

So if we are fairly to test the sensitivity of the inflamed appendix we must remember the necessity for mass stimulation. The stimulus I have selected is a squeeze applied to the appendix by grasping it between thumb and three fingers, usually of one hand, sometimes two. Squeezing as great a length of the appendix as possible not only imitates the natural adequate stimulus, but it corresponds with that applied in clinical examination—viz., the pressure of the palpating hand. It has been noted that whereas a squeeze may cause no pain when applied over two or three millimetres by the blades of a forceps, definite pain may result when a squeeze is applied by hand as described above. Visceral sensibility is of a comparatively low order. The viscera differ from the body surface as to sensibility in the same way as the skin surface differs from the cornea. The cornea is more richly supplied with pain nerves, and a piece of grit placed thereon will cause pain, whereas the same stimulus may cause no sensation when applied to the skin.

The influence of massive stimulation is illustrated by the well-known fact that hot water appears hotter to the skin the larger the area immersed in it.

Seventeen patients were investigated, all with marked deep tenderness. In 14 of these, pain resulted from squeezing the appendix, and no pain resulted from squeezing ileum and cæcum. In 2 cases of acute catarrhal type the results of the experiments were not definite. Both these patients had had morphia. The remaining patient, with auricular fibrillation and a gangrenous appendix, who had been given morphia ($\frac{1}{4}$ gr.), was in such a toxæmic state that he could be roused only with difficulty and gave no response to squeezing the appendix. It appeared that the abdomen could have been opened without local anæsthesia. This case made it clear that the morphia should be omitted if the investigations were not to be invalidated.

The painful appendices included all acute types, obstructive and non-obstructive, from the early acute catarrhal type (reddened and thick and stiff) to the partly gangrenous organ filled with fæco-pus and obstructed by a fæcolith.

The pain was central in nearly every case—in 7 umbilical, in 1 all over the abdomen, in 1 it appeared first on the left side and then in the middle, in 1 it was referred to the right iliac fossa.

It may be suggested that the reference of pain to the middle line on stimulating the appendix and its mesentery may be on account of the parietal anæsthesia

in the right iliac fossa, the pain being referred to the middle line by an experimental allocheiria, whereby the mind refers a stimulus from a region of lesser sensibility to one of greater. I do not believe the parietal anæsthesia to have disturbed the pain reference in this way, because the pain from stimulation of the posterior parietal peritoneum was usually localized in the right iliac fossa.

THE SENSITIVITY OF THE INFLAMED VISCUS

John Hilton in 1863, James Ross in 1888, and Henry Head in 1893, recognized the existence of both somatic and splanchnic elements in visceral pain.

Later observers, at the end of the nineteenth century and at the beginning of the twentieth, led by James Mackenzie and K. G. Lennander, noted the insensitivity of the viscera to ordinary pain-producing stimuli and they denied a direct splanchnic element in pain and tenderness. They referred the pain and tenderness to the body wall, Mackenzie by his visceroparietal reflexes, Lennander by direct mechanical or inflammatory contact.

In 1911 A. F. Hurst pointed out that pain may arise in a viscus if an adequate stimulus is provided. The only stimulus which he would admit as adequate was a disturbance of motor function causing abnormal tension in the muscular coat. He explained tenderness by Mackenzie's visceroparietal reflexes.[2]

In 1928 the author attempted, firstly to restore not only pain but also tenderness to the viscus; and secondly, to group inflammatory changes with motor changes as being a possible adequate stimulus.[9, 10]

In 1929 A. F. Hurst changed his position with regard to ulcer, admitting that tenderness may come direct from the lesion. He made the admission timidly, touching merely on the serous coat. This is strange, because the nerve-plexuses lie between and within the muscle layers. It is strange also that tenderness, and not pain also, should come directly from the lesion.[11]

In 1930 A. J. Walton expressed his belief in the importance of the inflammatory tissue as a direct cause of the pain of duodenal ulcers.[12]

In 1931 John Morley admitted visceral pain and denied visceral tenderness (thus conniving, as did Hurst, at an unnatural divorce between pain and tenderness). He also denied the visceroparietal reflexes of Mackenzie and admitted only the parietal peritoneum as being the source of the reflexes. He also denied to the inflammatory visceral lesion any pain sensitivity.[8]

The above position is confused. Much of our modern outlook upon abdominal pain, including the conceptions of Mackenzie, Hurst, and Morley, is based upon Lennander's conception that the viscera can in no circumstances be tender. It is important, therefore, that this pioneer work should be reviewed.[13, 14]

A study of the work of Lennander reveals five points which call for comment :—

1. He used morphia as a routine premedication. Morley also operated upon patients under the influence of morphia. But it must be remembered that morphia has a powerful effect in abolishing pain and its associated reflexes, and that this effect is almost specific with regard to the less intense pains of visceral origin. Powerful as is its effect in abolishing pain, in prevention of pain it is still more potent, so much so that surgeons who use local anæsthesia find pre-operative use of morphia an essential in all but the simplest operations. The following case is an example of its effectiveness, particularly in the very ill and debilitated patient.

Mrs. Annie W., aged 68, was admitted to St. Vincent's Hospital on March 2, 1936, complaining of epigastric pains for twelve months, jaundice for two weeks, and very severe attacks of griping pain in the epigastrium and right hypochondrium, with vomiting for one week. She was pyrexial, with a pulse-rate of 140, crepitations at the lung bases, and heavy glycosuria. The glucose-tolerance tests revealed diabetes mellitus. After three days pre-operative preparation she was given ½ gr. omnopon, $\frac{1}{200}$ gr. scopolamine, one hour before her operation. Field-block of the epigastrium was then carried out after the manner of Finsterer, and then without any further anæsthetic the gall-bladder was removed, two stones tightly impacted in the lower end of the common duct were removed, and then the lower end of the duct was dilated by passing Hegar's dilators up to No. 11/14 into the duodenum. These last manipulations necessitated a good deal of operative force and of mechanical retro-peritoneal disturbance, but they were not felt by the patient, although she would respond when spoken to.

It is possible painlessly to fasten a towel clip to the skin of a patient who has had morphia.

2. He used cocaine as a local anæsthetic. The curious general effect of cocaine, the euphoria which it produces, and its power of preventing and abolishing the unpleasant sensations of fatigue, suggest that it may have some inhibiting influence upon unpleasant sensations arising from the viscera, i.e., upon sympathetic afferents generally.

3. In anæsthetizing the abdominal wall, Lennander was much handicapped by the necessity of strictly limiting the dosage of cocaine, with the result that his patients suffered a considerable degree of parietal pain. Somatic response to mechanical stimuli is much more intense than visceral response, and so the visceral response may have been overshadowed by the former—the masking of the lesser pain by the greater. The importance of the above three factors is well seen in contrasting Lennander's results with mine in our investigations on the mesentery.

4. The conditions in which Lennander found the inflamed viscus to be insensitive were chiefly conditions in which we would expect the symptoms to arise either from irritation of the parietal peritoneum or from disordered peristalsis, and in which the visceral inflammation was of such a nature that we could hardly expect it to play any direct part in causing the pain. In short, it is of no use looking for visceral tenderness at operation, if there is none before operation.

In considering pain mechanism, it is most important to separate the painful and the painless types of inflammation. They can be distinguished, on the whole, by the tissue hardness or tension in the painful types. Thus, a gastric ulcer is typically painless when acute, but may be painful when it becomes chronic and indurated. An acute gastritis is typically painless. An acute appendicitis is usually painful, because the anatomical conditions permit a rise in tension in the tissue. The appendix has a relatively thick wall and narrow lumen, and is enclosed in a peritoneal sleeve which is not physiologically adapted to permit great and rapid increase in the volume of its contents. An acutely inflamed segment of intestine is not tender (in enteritis the pain is peristaltic, and in generalized peritonitis it is parietal in origin), until actual induration occurs. Again, a cellulitis is usually painful and the tissues are tense, but it may be painless in loose tissues. There is a hard painful type of carbuncle with much skin over it, and a soft painless type in which the skin soon disappears revealing a gelatinous tissue beneath. Compare also the tissues before and after incision of a painful tense abscess.

5. He did not recognize the necessity for massive stimulation when investigating visceral disease. In a few cases in which he applied pressure to the greater

part of the viscus, pain resulted (e.g., *Case* 5 in his 1902, and *Case* 5 in his 1904, publication).

The evidence which shows that the viscera may be directly sensitive to pain and tenderness in certain pathological conditions is as follows :—

1. Clinicians get the impression in examining the abdomen that the diseased viscus may itself be tender. However, as Mackenzie pointed out, sensitive parietal tissues intervene and the area of tenderness does not necessarily correspond with the outline of the viscus. He demonstrated a tenderness in the parietes. But this does not rule out the possibility of visceral tenderness also, nor does it justify lightly dismissing the clinical impressions of generations of physicians.

2. Cases are sometimes encountered in which there can be no contact between the abdominal wall and the lesion. These cases cannot be explained by Morley's anterior parietal peritoneum theory. Cases in which the tender viscus is felt per rectum or per vaginam can be explained neither by Morley's theory nor by Mackenzie's visceroparietal reflexes. Thus, the viscus itself is left as the direct cause of pain in these particular cases. Examples are given as follows :—

Mr. M., a middle-aged man, was admitted to the Pembury Infirmary (Kent) in 1930, complaining of weakness, indigestion, swelling of the legs, and shortness of breath, suggesting cardiac failure. He had a localized, deep tender area in the epigastrium. This proved to be so constant and so marked that I operated upon him in spite of a negative radiological report, and found a large ulcer of the anterior wall of the stomach, near the lesser curvature, penetrating deeply into the liver. It was separated from all possible contact with the anterior wall of the abdomen. The whole of the gastric area of the liver was firmly adherent to the anterior surface of the stomach, so that there was no possibility of the examining hand displacing the liver margin and bringing the lesion into contact with the anterior parietal peritoneum. The lesion was separated from the posterior parietal peritoneum by the posterior wall of the stomach. The lesser sac was free, and a posterior gastro-enterostomy was carried out. The patient improved markedly.

Master Th., aged 12 years, came into Hornsby Hospital under my care, in 1936, complaining of central abdominal pain for 32 hours. The house surgeon and also a highly competent senior practitioner concluded, from the complete absence of abdominal tenderness, that the case was one of simple intestinal colic. A slight rise of temperature prompted me to mistrust the diagnosis and visit the patient. Examination of the abdomen revealed no tenderness, but examination per rectum revealed a very tender mass in front of the rectum, and a diagnosis of pelvic appendicitis was made. Operation was carried out through a right paramedian incision, a lot of free turbid peritoneal exudate appeared, and the appendix was found in the rectovesical fossa. It was offensive in odour, distended by fæco-pus, and contained a large hard fæcolith. The tenderness must have been truly visceral.

3. The peculiarities of the pain and tenderness of peptic ulcer cannot be accounted for unless the sensitivity of the actual lesion is admitted. The gastric acidity shows no significant changes in the pain periods as compared with the free intervals. The effect of introducing acid into the stomach of patients with ulcer is variable. The motor activities of the stomach show no characteristics peculiar to the pain periods. These points have been discussed more fully in an earlier communication.[9] The difficulties encountered through failing fully to realize the sensitivity of the actually inflamed tissue are well illustrated by Hurst's efforts to explain the pain and tenderness. Hurst[2, 11] explains the pain of ulcer as being due to unusually powerful peristaltic waves battering against a spastically closed pylorus at such a rate and with such constancy as to produce a continuous pain, and "the rise in pressure in the pyloric vestibule produces an abnormal degree of tension in the individual fibres of the muscular coat of this segment of the stomach.

This is the actual cause of the pain, the rise in tension being the adequate stimulus required to produce the afferent nervous impulses which give rise to the sensation of pain." And so, spontaneous pain does not arise directly in the ulcer. But while denying direct ulcer pain, Hurst, since 1929, has admitted direct ulcer tenderness. (Before this he looked upon the tenderness as parietal and explained by Mackenzie's reflexes.) In other words the induced pain comes from the ulcer, but the spontaneous pain does not. This is an amazing inconsistency. It becomes still more difficult to understand when one remembers that the great bulk of radiological observation shows that the motor behaviour of the stomach shows no characteristics peculiar to pain periods. To make matters still more confused, Hurst confines his tenderness to the subserous layer of the bowel wall, although we know that the nerve-plexuses lie between and within the muscular layers. Hurst can hardly right his position except by unreservedly admitting that in peptic ulcer the ulcer itself may be both painful and tender. J. A. Ryle[15] gets into similar difficulties. He protests that peptic ulcer does not cause pain directly, because "gastric pain, closely similar to and as severe as the pains of gastric and duodenal ulcer, can occur in the absence of a gastric or duodenal lesion". (Let us apply this reasoning elsewhere—some cases of astigmatism are associated with frontal headache, other cases of frontal headache are not associated with astigmatism, therefore astigmatism does not cause frontal headache directly!) Ryle is forced to conclude that "it" (hunger-pain) "does not express these (gastric and duodenal) lesions, but only the nervous perturbation of function which they are liable—as foci of irritation—to engender". Not only is his reasoning at fault, but his premises become more doubtful as knowledge increases. Schindler and others have shown by gastroscopy that many of these cases without ulcer are actually cases of hypertrophic gastritis. And others are cases in which the ulcer has remained hidden (e.g., on the posterior wall or between the layers of the mesentery). In one case the symptoms were said to be due to the "nervous perturbation of function" brought about by an epigastric hernia, and the cure of the epigastric hernia was thought to have cured the symptoms. But the symptoms soon recurred and the ulcer was searched for and found at a second operation.

4. Incontrovertible evidence of visceral tenderness is provided by those cases in which direct manipulation of the diseased viscus causes pain. This evidence includes: (*a*) The cases of appendicitis described in this paper; (*b*) The tenderness of the inflamed cervix uteri, which contrasts markedly with its insensitive condition in health; (*c*) The striking case, described by Dragstedt and Palmer, of laparotomy for duodenal ulcer under local anæsthesia. "The abdomen was opened and the stomach exposed with a minimum of discomfort. At this time he felt no ulcer distress. A puckered scar was visible on the anterior wall of the duodenum about 1 cm. distal to the pylorus. On very gently rubbing the serosa over this scar with the gloved finger, the patient complained of pain similar to his ulcer distress. This pain persisted after the rubbing was discontinued. The patient was then told that something would be done to entirely relieve his distress, whereupon the region of the ulcer was rather firmly compressed between the thumb and forefinger of the operator and massaged gently but firmly. This produced severe distress."[16]

5. In three of the acute appendicitis cases investigated the patient's pain disappeared in dramatic fashion when the mesentery of the appendix was blocked with novocain.

THE MECHANISM OF PAIN PRODUCTION IN PEPTIC ULCER

Clinical and experimental observations in somatic and visceral disease show that excessive tension in the tissues is an adequate painful stimulus. The liability of the tissues to excessive tension is influenced by their texture and by their capacity for mechanically accommodating an increase in any of their constituents.

The tissue tension can be increased by cellular infiltration, by œdema, and by vascular engorgement.

Perhaps inflammation alters the reaction of the tissue fluids and has some chemical influence on the sensitivity of the nerves. In the tense congested tissue with inefficient circulation, one would expect the acidity of the tissue fluids to rise, and to fall again as the efficiency of the circulation improved and the congestion became less through the opening up of collateral channels, as for example by the foment applied to the boil, or by the physiological hyperæmia which occurs in the stomach in response to the ingestion of food. The experiments of R. M. Moore lend support to this possibility. He observed the effect of injecting various solutions into arteries, and noted that pain-endings are found to be sensitive to a degree of acidity which is attained in ischæmic tissue. No doubt other chemical alterations, besides those in acidity, take place.

Of course the ultimate capacity for pain production by increased tissue tension and by alteration in tissue fluids depends upon the number and the nature of the nerve-fibres in the tissue.

The bearing of these principles upon the pnia of peptic ulcer and their correlation with the secretory and motor functions of the stomach, have been discussed at length in previous communications, and the difficulties caused by their neglect have been pointed out already in this paper.

The cerebrospinal and the autonomic nervous system are not two separate nervous systems. They are merely branches of the one nervous system. Their essential unity will be discussed later, but the similarity of their responses to inflammatory lesions may be stressed here :—

1. In the earlier stages of its development a boil on the forearm is painless—as is also a gastric ulcer. Tissue tension and alteration in chemistry of tissue fluids have not reached a degree necessary for pain production.

2. In an intermediate painful phase, the pain is profoundly modified by alterations of the circulation, as follows : when the arm is kept at rest and elevated, the pain of the boil disappears ; when the stomach is kept empty and at rest the pain of ulcer disappears.

3. If the patient with the boil causes a hyperæmia of the forearm by lowering the arm, and then, by clenching the fist, squeezes blood out of the muscles so as visibly to increase the congestion in the subcutaneous veins, severe pain results. With regard to the stomach, we can induce a hyperæmia by giving the patient a meal. As the stomach empties, and squeezes down on its capillary bed, during this digestive phase, blood is forced into the unyielding ulcer tissue, and changes in tissue tension (and perhaps in the chemistry of tissue fluids) result, and cause pain.

4. Now let us open up the surrounding capillaries and induce a more rapid and efficient circulation in them, by a fomentation on the forearm, or a glass of milk and some bread and butter in the stomach. The pains are relieved.

5. As time goes on the pathological hyperæmia of the two lesions diminishes, in the boil through the separation of a slough and the discharge of pus, in the peptic ulcer through influences which we do not thoroughly understand (perhaps through seasonal fluctuations of bacterial activity). At any rate the lesions remain with their breach in the epithelial covering and their zone of inflamed indurated tissue—but both lesions enter upon a painless phase. (The author has been able during the last few weeks to confirm personally these phases in the furuncle of the forearm.)

THE SUPERFICIAL AND DEEP TENDERNESS OF PEPTIC ULCER AND THE VAGUS

In 1929 I drew attention to two types of tenderness in patients with peptic ulcer (*Fig.* 332):—

1. The superficial tenderness, more marked in 'nervous' patients, present in the gastric neuroses, and independent of any change in the position of the stomach. This tenderness is found in the epigastrium, and includes the whole or part of this region, usually the whole. C. Bolton[17] has confirmed the existence of this type of tenderness and has noted that it may be found, not only in the epigastrium, but also in more posterior parts of the same dermatomes. This tenderness obviously depends upon a viscerosensory reflex subserved by the sympathetic visceral afferents.

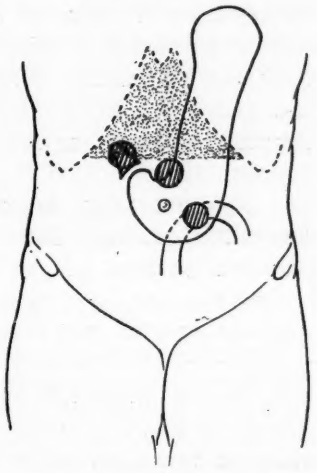

FIG. 332.—Distribution of tenderness in peptic ulcer. The superficial tenderness is stippled. The deep tender points (gastric, duodenal, anastomotic) are represented as shaded discs.

2. The other type of tenderness is deep, and sharply localized. It can only be elicited when the actual lesion is pinned down. It is found even in phlegmatic types. The situation of this tender point varies with the position of the viscus. With the patient supine, it may lie beneath the zone of superficial tenderness and move down below it when the patient stands up. Its characteristics have been confirmed by John Morley and E. W. Twining.[18] It is a true visceral tenderness. It is interesting to speculate as to whether the vagus can play any part in its conduction. Lennander held that the vagus below the inferior laryngeal branch does not mediate pain. This has not been proved, and the evidence is conflicting. At least we know that the sacral autonomic mediates pain conduction, and we may expect the cranial autonomic to do the same. In 1928 I described a patient with a complete transverse lesion of the cord at the level of the third thoracic vertebra who felt enema pains. Alvarez (personal communication) refers to a similar case of Foerster's—a patient who had a transverse myelitis and who yet felt gall-bladder pains.

I have to thank Mr. R. A. Money who recently gave me the opportunity of examining a patient under his care. This man had a complete transverse lesion of the spinal cord, at the level of the third thoracic segment, afterwards proved to be due to an extramedullary nodule of metastatic carcinoma, possibly from the prostate gland. Two days after laminectomy and removal of the tumour he was

given cascara. He was conscious of the bowel movements within the abdomen. They were not painful. At this time he had shown no signs of recovery of cord function.

The question of the part played by the vagus in conveying sensation must be looked upon as still an open one.

TENDERNESS AND MUSCULAR RIGIDITY OF PURELY VISCERAL ORIGIN

Mackenzie and hosts of physicians and surgeons have looked upon tenderness and muscular rigidity as depending upon a visceroparietal reflex. Professor Morley vigorously denies this explanation and states in his book that " when pure visceral pain occurs, it is entirely unassociated with any tenderness, superficial or deep, or with any reflex muscular rigidity of the abdominal wall." Professor James Young[19] made a similar statement, and prints it in italics in his address.

In this way, Professor Morley and Professor Young illustrate a tendency amongst investigators of abdominal pain to make certain observations, and then most unjustifiably to claim that the subject is a simple one, explained entirely by their own postulates. Rather is it to be believed that the subject is a complex one, that there are many factors involved, that patients differ constitutionally and clinically, and that the relative importance of the various factors differs in different patients.

The following experiences support the older visceroparietal reflexes of Mackenzie, without however prejudicing the importance in other cases of the peritoneal reflexes.

On June 9, 1937, at 4 a.m., I saw Mr. S. R. S. aged 46, in his home. He had been awakened from his sleep at 12.30 a.m. by violent upper abdominal pain. He gave a history of previous epigastric pain, before meals, relieved one year ago by a course of alkali. Examination showed extreme tenderness and rigidity of the upper part of the abdomen, especially to the right. A diagnosis of ruptured duodenal ulcer was made. Laparotomy at Hornsby Hospital at 6.30 a.m. showed the abdominal organs to be normal, except the gall-bladder, which was very tense, but not enlarged. It was full of stones of moderate size, but these were quite impalpable until the gall-bladder was aspirated. The peritoneal covering of the gall-bladder was smooth and shiny, the wall was normal and translucent, and showed no signs of inflammation. Cholecystectomy cured the patient. The point to be noted in this case is that the marked tenderness and rigidity were observed three and a half hours after the onset of the attack of biliary colic, i.e., before one would expect to find any peritoneal irritation. In point of fact laparotomy two and a half hours later showed that even then there were no signs of peritoneal irritation.

On August 22, 1938, Wm. Eth., male, aged 39, in Hornsby Hospital, had a very severe epigastric pain of six hours' duration, and was markedly tender with board-like rigidity in the upper part of the abdomen, especially over the right rectus. There was no cutaneous hyperæsthesia. I believed that he was suffering from biliary colic. But I had recently read Professor James Young's article and had again studied Professor Morley's book, and so I could not reconcile my diagnosis with marked tenderness and rigidity. Further, the house surgeon had made a diagnosis of ruptured peptic ulcer. Urgent laparotomy revealed a small gall-bladder covered by the liver and not making any contact with the parietal peritoneum, normal in appearance, but filled with tiny calculi. There was no other lesion. Cholecystectomy cured the patient.

A study of rigidity in acute appendicitis has proved of interest. In 15 cases operated upon by the author in which the rigidity was very well marked, 14 had free fluid in the abdomen. The exception was a gangrenous appendix lying over

the pelvic brim. Free fluid therefore appears to be of importance in causing rigidity. But the exception proves that there are other factors. Then, the cases are not uncommon in which there is a little or no rigidity, and yet free fluid, varying from clear to frankly purulent, is found.

SUMMARY

1. The effect of parietal anæsthesia has been investigated, and the observations of earlier workers confirmed.

2. The anterior parietal peritoneum was invariably sensitive. In most cases it localized the stimulus accurately. The work of Lennander was thus confirmed.

3. The sensibility of the posterior parietal peritoneum of the right iliac fossa has been investigated in 19 cases: in 10 it was insensitive; in the other 9 its stimulation caused pain, referred in most cases to the right iliac fossa.

4. The nerves of the mesentery of the appendix were uniformly sensitive to physical stimuli, and pain was referred to the middle line in most cases.

5. The acutely inflamed, clinically tender appendix was directly squeezed in 17 cases: it was tender in 14; 3 cases, which had had morphia, were not definitely painful.

6. The sensitivity of the inflamed viscus is discussed.

7. Pain in peptic ulcer is discussed.

8. A distinction is made between two types of tenderness in peptic ulcer.

9. The visceroparietal reflexes of Mackenzie are defended.

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THE REMOVAL OF LARGE SPLEENS

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THOUGH my own experience of splenectomy is barely moderate by the measure of Egypt, eleven years at Kasr el Aini Hospital have left me with certain convictions about the operation; for there, large spleens—like sorrows elsewhere—" come not single spies but in battalions", and my friends and former colleagues who work in this profusion will know these notes were made for other lands. But, while it is, for example, a privilege and stimulus to see H. E. Stiven removing—as he did so admirably during the Congress of 1935—six spleens in a morning, it is also well for occasional splenectomists to weigh a counsel which runs as follows :—

> Most operators gain increasing respect for splenectomy the oftener they are called upon to carry it out. When the organ can be lifted out of the abdominal incision, the operation may be one of the easiest and safest in surgery. But when there are diffuse, firm adhesions, the bleeding is often terrific and the operation most dangerous. In fact, in many of the latter cases it would probably be wiser to abandon the attempt to remove the spleen and to be content to diminish its activity by ligaturing as much of the pedicle as can be safely reached. (G. GREY TURNER, *Modern Operative Surgery*, I, 704.)

Such prudence from an established source of surgical courage may well serve me for preface.

I shall first consider the operation under traditional headings: (1) Incision; (2) Mobilization and delivery of the spleen; (3) Treatment of the pedicle; and then deal with an observed effect of removing large spleens on the function of the diaphragm. I have put details that might burden the text in footnotes and legends.

INCISION

With proper relaxation any spleen can be removed through a paramedian incision, and I have used no other. It should, however, comply with definite conditions. First, it must reach the costal margin itself; every inch short of that margin will seem an ell of handicap in delivering difficult spleens. Beginning then at the left margin, three finger-breadths from the middle line, the incision reaches a point three finger-breadths beyond the caudal end of the spleen. The rectus sheath is opened, and the muscle, displaced outwards, acts later as a truss, perhaps superfluous above the navel but welcome below. The sole *addition* to this approach that I can think useful is a transverse section of the abdominal wall. This supplement, which might give good access in the absence of relaxation or proper means for dealing with adhesions, leaves no excuse for dividing the cage of the thorax during splenectomy.

I am not sure, however, that I might not revise my outlook on the question of incisions were I once more in the ambit of large spleens, for the great increase of the subcostal angle—sometimes to almost 180°—that often goes with them, offers perhaps a path leading directly through the heightened loin to the *hinder* face of the pedicle, and I shall deal presently with the use of this posterior aspect.

MOBILIZATION AND DELIVERY OF THE SPLEEN

After a round of inspection the surgeon proceeds to deliver the spleen; omentum may cover or bind the lower portion which presents first, and the novice, exposing this part of the organ, will take the primrose path and lift the spleen out by the tail—an act indifferent with small specimens, but quite otherwise with the large, whose cephalic pole or 'head', outgrowing the rest, will often bulge the left cupola and fill the whole expansion of its cavity; in this way a major mass of spleen is sheltered by the ribs in a deep, stiff-walled space that fits like a glove. The novice then (as I found), by lifting the tail up, cants the big head firmly down into this space and jams it undeliverably. The moral is clear: *Bring the 'head' out first*, and spleens—like sheep—will carry their tails behind them.

But splenic adhesions are common, and those to the dome of the diaphragm or to the costal origins are sometimes dangerous to tear if the spleen hides them from view. Often they are frail and easily broken with the fingers; frequently they form thick bands, and sometimes the spleen is almost felted to the cupola: firm attachments like these have put a stop to many splenectomies.

Faced one day in 1930 by a case with multiple and dense adhesions, my then colleague, Dr. F. Yusry, F.R.C.S., suggested dividing them with the high-frequency current. This was done rapidly, keeping close to the spleen, and the patient, who was otherwise inoperable by the far from timid standards of Kasr el Aini, surprised us with a smooth recovery. But really we should not have been surprised, for this diaphragm was much less damaged than others with adhesions blindly clamped in the crevice between cupola and spleen. Since then I have performed no splenectomy without first fastening a broad electrode to the patient, and instead of wasting time dangerously with clamps I divide tough, invisible adhesions with the current.

Frail adhesions, too, have their dangers, for they are so easily broken as to give a treacherous feeling of security; on rare occasions they bleed thereafter with a slow, unspectacular persistence, and the volume lost is only noticed when the spleen is out and away. It should thus be delivered rapidly, and if tough adhesions mix with the frail, the high-frequency current will soon finish separations begun by the hand.

Before we thought of the current a patient of mine died of hæmorrhage concealed by a spleen too slowly delivered, and since then there have always been prepared for my splenectomies a small vessel for baling blood from the abdominal cavity, and means of filtering it and restoring it to the patient's veins. I have found Denis Browne's large metal syringe admirable for this purpose; it holds 600 c.c. of blood and citrate solution in the proportion of five parts of blood to one of 1 per cent sodium citrate in water:* the blood can be filtered directly into its wide barrel through two lazers of gauze (*Fig.* 333).

TREATMENT OF THE PEDICLE

In my experience hæmorrhage from the splenic pedicle, which a firm grasp will check, is more troublesome than dangerous, but may sometimes deface the field or disturb the mind. The friable veins are often the size of a thumb, and are

* I learnt from my former colleague, Colonel A. G. Biggam, to keep the citrate conveniently in the theatre in sterile gramme doses of the dry salt sealed into ampoules that are stored in lysol.

easy to flatten and skewer in the guise of harmless, avascular parts of the pedicle; no *blind* pass, therefore, should be made with any metal tool. The best instrument for finding unforcible passage is the index finger, whose gentle emergence is only counted safe when the true tint of the glove shows through a last coat of peritoneum: a curved forceps—passed back through the pedicle in contact with the retreating index—retrieves the ligature. It is not always well to insist on cleaning these large veins too thoroughly before tying them; on this account they should not be tied with catgut, for the ligatures must be drawn tight enough—without fear of breakage—to hold the vein through tissues round it; silk or thread will do this best.

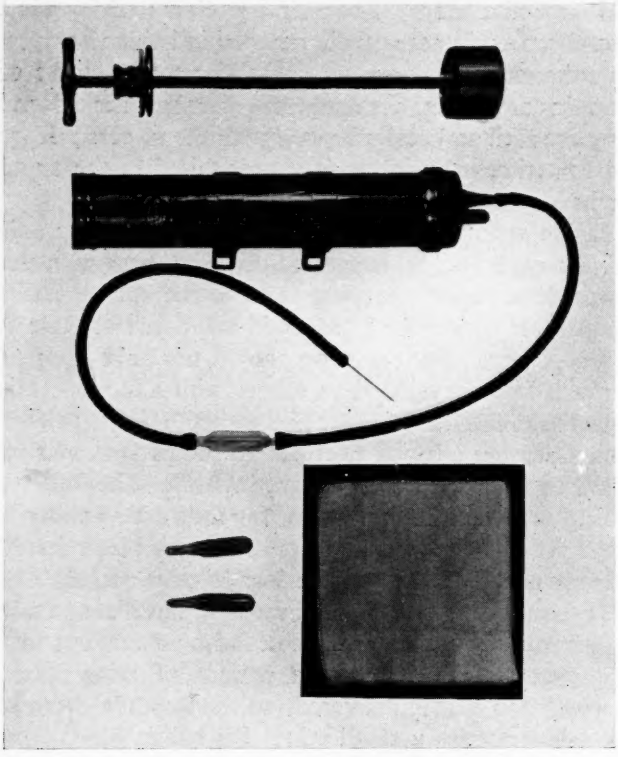

FIG. 333.—Denis Browne's apparatus, useful for collecting and citrating blood shed during splenectomy and returning it to the patient's circulation. The fine thread of the screw on the piston-rod allows of gradual intravenous injection. The ampoules, stored in lysol, contain 1 g. each of solid and sterile sodium citrate. The gauze layers filter blood baled into the upright barrel of the wide syringe, which holds 500 c.c. of blood and 100 c.c. of 1 per cent watery solution of sodium citrate.

Clamps.—Many, I think, reserve clamps and forceps for the *distal* ends of these frail vessels, and wisely tend with experience to use for the pedicle the old and cautious plan of two intrepid surgeons, ligating piecemeal in the manner of Ali Ramez and Owen Richards.

Choice of Route.—After these generalizations, two ways of attacking the pedicle must be considered in detail—the common, but vaguely charted, approach from in front, and the rather neglected posterior route.

Since Balfour's paper in 1916, the posterior route is mentioned in descriptions that either treat lightly or leave out the strong reasons for using it. Balfour's primary object was to peel the tail of the pancreas easily off the spleen, but in my

experience the posterior approach has been first and foremost a short cut to the splenic vessels. A back view of the pedicle is, therefore, a thing to welcome and

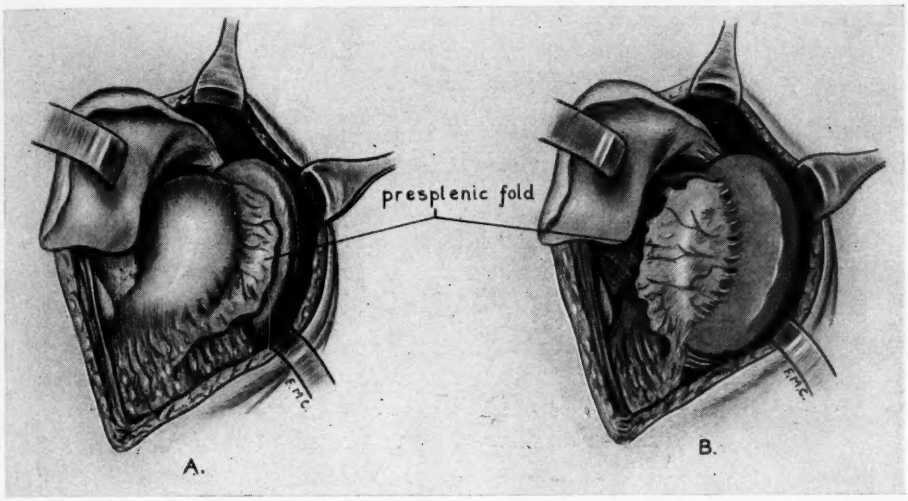

FIG. 334.—*Presplenic fold*: A, seen from in front; B, turned medially. This fold, which is often present, springs from in front of the great omentum and overlies the gastrosplenic ligament; normally free at its left border, it forms attachments to pathological spleens, especially at the lower pole, and carries vessels of the left gastro-epiploic group. Its distal edge is often the first thing divided when approaching the pedicle from in front. (*See also Figs.* 336, 339, and 340). The presplenic fold and gastrosplenic ligament tend normally to lie antero-posteriorly, but when the spleen enlarges they are carried forwards to occupy *frontal* planes.

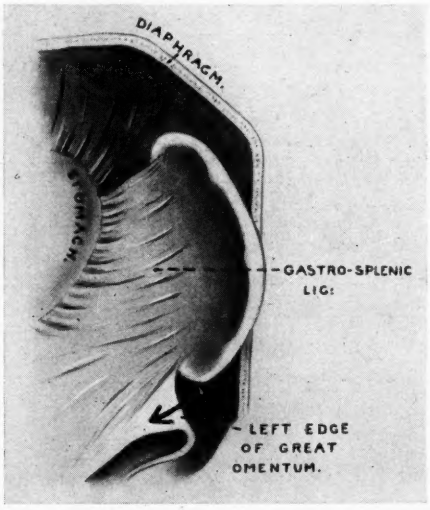

FIG. 335.—The continuity of splenic ligaments and great omentum (*see also Fig.* 338). In this figure, drawn from an infant subject, the lumen of the lesser sac is still present within the great omentum. The two anterior layers of the left portion of omentum continue into the gastrosplenic ligament; the two posterior layers into the lienorenal. The presplenic fold is absent. The arrow shows the path taken by enlarging spleens round the omental edge, and this edge may adhere to the spleen and simulate a presplenic fold. (*After Testut.*)

exploit. It is obtained with large spleens in about three patients out of ten, but is perhaps more often available in this country where spleens range small, for in three of the four splenectomies that have come my way in London I was able to use a

posterior approach to the pedicle. Its value appears from the following contrast. The common, and often the only possible, route is, of course, through the front of the gastrosplenic ligament which contains left gastro-epiploic vessels that join the large spleen, forming a kind of false, and frequently fat-laden, pedicle.*

A leash of veins from the lower pole belonging to this series frequently runs in a *presplenic* fold (*Fig.* 334). This fold—seen but not named in Symington's *Atlas* of cross-section anatomy—is well represented in a specimen from Professor Grey Turner's private collection (No. T, 2329), where it is double. Often small and trivial, the fold may greatly increase and fill with fat in splenomegaly, adhering to the large spleen and thickening the pseudo-pedicle. Sometimes, too, the tail of the spleen, descending as it grows, comes round and draws down the edge of the great omentum which sticks to it, and this edge may simulate a presplenic fold (*Fig.* 335). Many splenectomies begin with ligation of one or the other of these peritoneal structures.

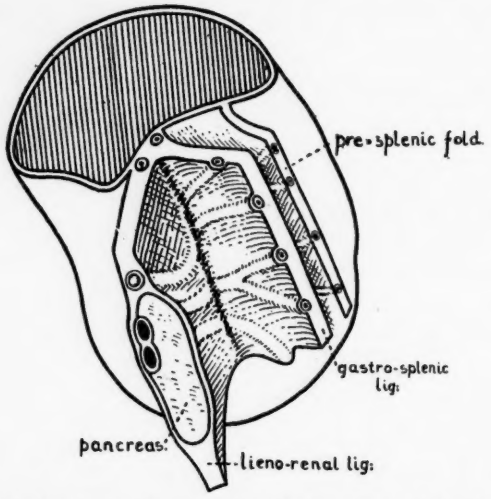

FIG. 336.—Diagram showing the constituents of the splenic pedicle. A *presplenic fold* is seen adhering to the enlarged spleen: this fold, with the *lienorenal ligament*, constitutes a false pedicle carrying vessels derived from the left gastro-epiploic vein and artery in addition to vasa brevia from the splenic trunks. The layers of the lienorenal ligament here include the tail of the pancreas, and this ligament is called *pancréatico-splénique* in France. Sessile spleens (*Fig.* 339, C) have no lienorenal ligament. (*Modified from Paitre, Lacase, and Dupret.*)

Dividing either fold opens a path for the index finger, and this, used in the way described above, is the safest guide for passing ligatures round the vessels. Their piecemeal ligation carries the surgeon gradually through four peritoneal layers of pseudo-pedicle and brings him to the front of the lienorenal ligament (*Figs.* 336, 340). This ligament, which is called in France the *pancréatico-splénique* (*Fig.* 336), contains—in addition to odd splenuncules, lymphatic glands, and the tail of the pancreas—the true vascular pedicle of the spleen.†

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* The gastrosplenic ligament is not always fat-laden; the spleen, enlarging greatly, may so stretch the ligament from above downwards that a series of translucent areas separate its vessels close to the spleen and simplify their ligation. Rowlands and Turner give an excellent description of this appearance, which I have seen many times.

† The term 'presplenic fold' is taken from the admirable *Pratique Anatomo-Chirurgicale Illustrée*, by Paitre, Lacase, and Dupret. Theirs is the only account I know of splenic anatomy and splenic relations from a surgical standpoint worthy of Binnie's epithet, "soul-satisfying".

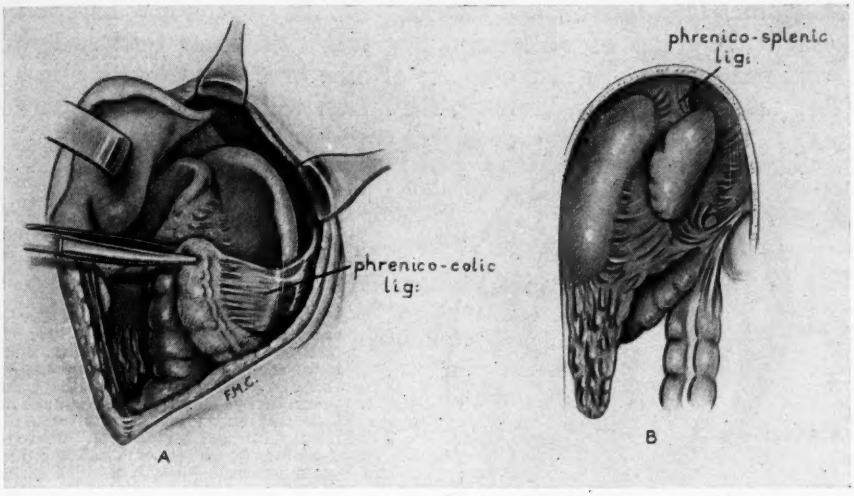

FIG. 337.—*Other peritoneal relations*: A, An exaggerated development of the phrenicocolic ligament which may give an abnormal direction to the enlarging spleen and keep it behind the transverse colon; there is then a misleading band of resonance on clinical examination *in front* of the splenic mass. B, The phrenicosplenic ligament, an occasional fold proceeding to the diaphragm from the junction of the lienorenal and gastrosplenic ligaments. This junction roofs the blind left end of the lesser sac (*see Fig.* 338).

The solitary figures seen in some text-books, appearing to suggest that all splenic pedicles can be clamped across simply and as a matter of course, remind one of specious advertisements.

Other peritoneal relations and attachments which are occasional will be found in *Fig.* 337, A: it too has been adapted from the *Pratique Anatomo-Chirurgicale*. *Fig.* 337, B perhaps explains how the splenic tail may be diverted into a retrocolic position as it grows caudally. I have twice found the transverse colon lying in front of a large spleen.

An Aide-mémoire to Splenic Anatomy.—I am sometimes surprised at the anatomical twilight in which many splenectomies thrive. Relations of spleen and peritoneum I know are confusing, but the briefest reference to embryology clears the picture.

The gastrosplenic and lienorenal ligaments both develop from the dorsal mesogastrium that slings stomach to spine and divides the upper part of the fœtal abdomen equally to right and left. Rotation of the stomach bends this mesogastrium—like a fallen < —into lienorenal and gastrosplenic portions.

It is easy to show by a living model the change thus produced in the vertical sling. Hold the left hand, thumb up, in line with the forearm. Let the hand (palm and fingers) represent the dorsal mesogastrium—the palm, its proximal part; the fingers, the distal: the stomach, of course, lies at their tips, and the spleen grows out from the metacarpal knuckles. Now flex the straight fingers at the metacarpo-phalangeal joints and dorsiflex the wrist. The fingers then simulate the gastrosplenic ligament; the palm—carrying the pancreas—is the lienorenal; the spleen, as I have said, grows leftward at the knuckles. When the mesogastrium bends like a < the dorsal vessels of the stomach which are inside it bend also; their proximal segments go to the left and become splenic vein and artery; their distal segments bend to the right in the form now of mere splenic branches and tributaries—vasa brevia, namely, and left gastro-epiploic vessels.

The length of the lienorenal ligament (which Testut, who knew it well, says Wiart never saw!) is given by Paitre and his colleagues as from 1 to 7 cm.; it is, they find, less supple, less extensible, "*less obliging to the surgeon*" than the gastrosplenic. The more fusion there is between the original left side of the dorsal mesogastrium—the back of the 'model' hand—and the parietal peritoneum covering the left kidney, the shorter the lienorenal ligament will be; it ceases to exist when fusion is complete. The French call it *pancréatico-splénique* because when the ligament is present it holds between its layers the tail of the pancreas.

The relation of the gastrosplenic and the lienorenal ligaments are well seen in *Figs.* 336, 338, which are taken from a subject with a long splenic pedicle like that in *Fig.* 339, A, and show the two ligaments continuous with one another round the left extremity of the lesser sac whose small blind end reaches the spleen and 'floats' with it in the great cavity of the peritoneum. When, on the other hand, spleens are sessile (*Fig.*339, C) this blind end is fixed to the posterior wall of the abdomen like the rest of the lesser sac.

Taking, therefore, the common anterior route the surgeon may have to find his way through five sheets of peritoneum that subdivide layers thickened with fat, glands, and pancreas, which in the course of time have caked together in a single mass (*Fig.* 340). Sometimes, however, the spleen will roll obligingly on its long

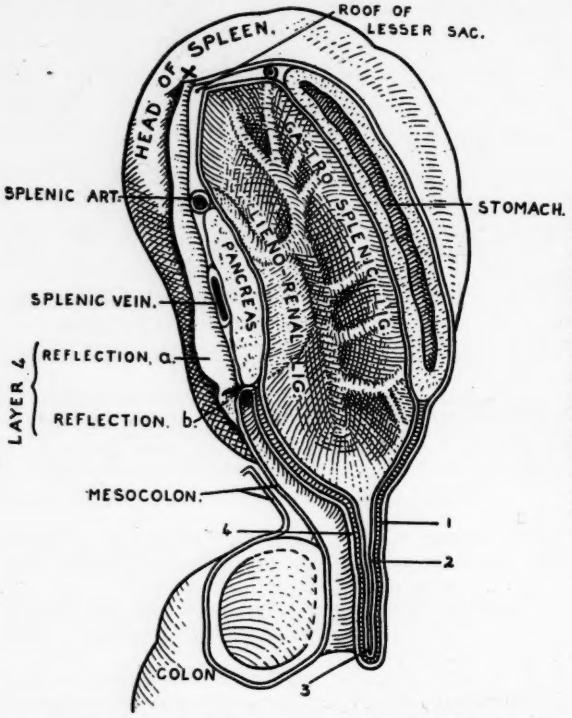

FIG. 338.—The left end of the lesser sac seen from within. The spleen here has a long pedicle (*Fig.* 339, A); the blind end of the lesser sac—which enters the pedicle—'floats', therefore, with the spleen in the greater peritoneal cavity. The gastrosplenic and lienorenal ligaments surround the blind end, their four layers meeting at X in its roof. Traced caudally these four layers are continued into those of the great omentum—1, 2, 3, 4. The *anterior* layer of the gastrosplenic ligament (layer 1), and the *posterior* of the lienorenal (layer 4) belong to the *greater* sac. Layer 4 curves off the tail in two directions at right angles to each other, *a* and *b*, leaving the back of the body of the pancreas bare of peritoneum: *a* is the reflection outward from the tail on to the kidney; *b*, the downward or caudal reflection from the lower edge of the pancreas. A fold may go from X to the diaphragm—the phrenicosplenic ligament (*see Fig.* 337).

axis over towards the surgeon as he stands on the patient's right; he is then fortunate, for instead of having to find major vessels in a kind of anatomical club-sandwich, they will at once present, either covered by a single posterior leaf of lienorenal ligament, or bare—as if dissected out by peritoneal rupture (*Fig.* 341).

So great is the advantage of working from the back of the pedicle that, even when the spleen will *not* turn readily over, the small trouble of taking a seat on the

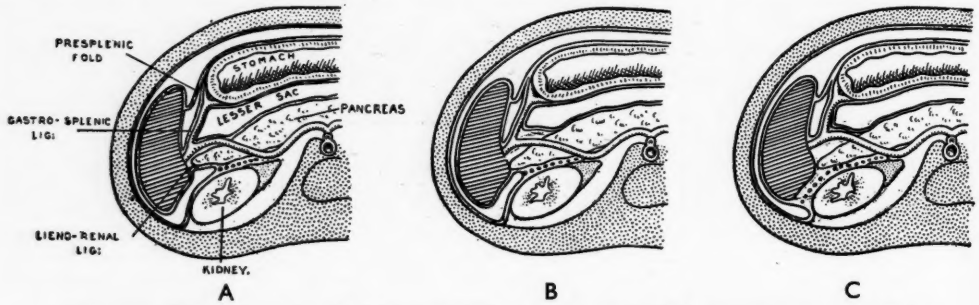

FIG. 339.—Three varieties of splenic attachment: A, The *long-pedicled spleen* which rotates on its long axis to the right and gives easy access to the back of the pedicle. Spleens, however, may be so large that axial rotation is checked by their own bulk. It is then that the surgeon can with advantage seat himself on the patient's *left* side in order to work on the back of the pedicle (*see* text). B, The *short-pedicled spleen*; C, The *sessile spleen*. These last two types can only rotate after rupture or division of the parietal peritoneum. The third type has no lienorenal ligament. (The dotted lines mark planes of embryonic fusion which are also planes of potential cleavage.) These figures are all diagrammatic; they omit the thick fat and fusion of layers, which can make the anterior approach so difficult.

patient's left and looking at the field from this low level will sometimes give surprisingly swift and dry splenectomies. But schedules of technique are suggestions,

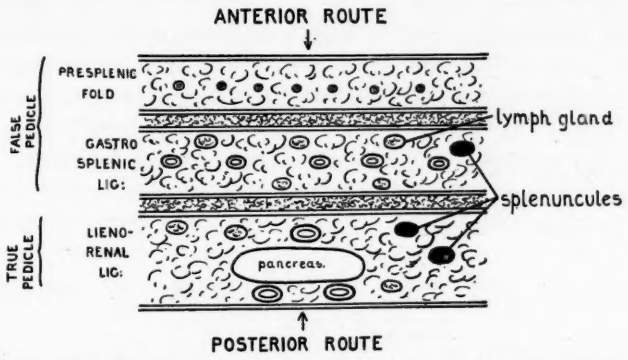

FIG. 340.—*The anatomical club-sandwich*: Diagram of a splenomegalic pedicle seen in sagittal section. The layers are thick with fat and caked together. This diagram affords a contrast between the anterior and posterior routes of access to the splenic vessels. (Rings represent vessels.)

merely for eclectic use, and sometimes vessels clear in fat-free peritoneum invite me to begin in front with the pseudo-pedicle; then if the spleen will turn, I work from the back.

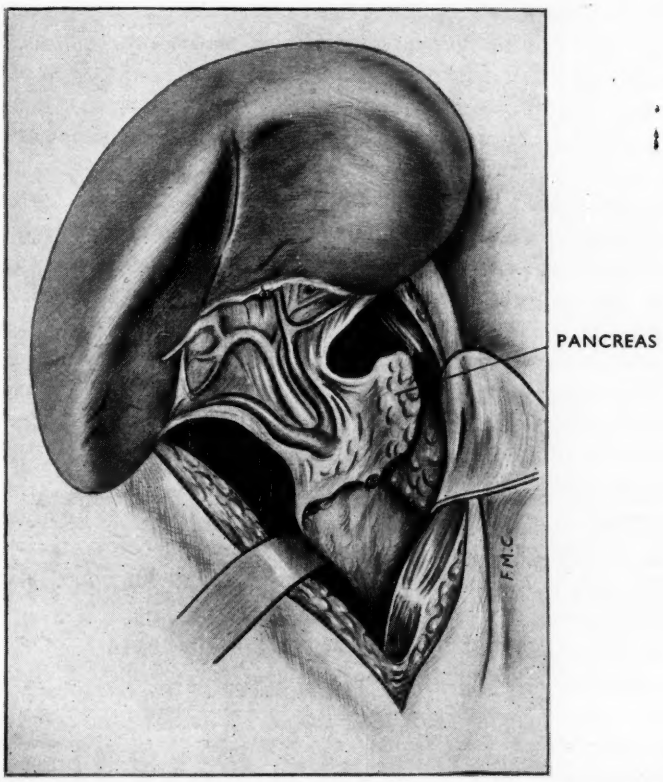

FIG. 341.—The pedicle approached from behind. The main vessels have been exposed here by dividing the single leaf of peritoneum which covered them—the posterior layer of the lienorenal ligament. This layer is often torn in mobilizing a short-pedicled spleen (*Fig.* 339, B); the vessels are then laid bare without dissection. (*After Balfour.*)

The Stomach and Pancreas.—The text-books warn against wounding the stomach in dividing the narrow cephalic part of the gastrosplenic ligament—a warning with special point if we approach the pedicle posteriorly; for when the spleen is rolled to the right the ligament winds with it and wraps the gastric wall.

The second hazard, the tail of the pancreas, has been mentioned already. Balfour sought to spare it by approaching from behind, and I am sure it is often divided from in front. As a rule, however, the part cut is only fibrous, or at worst leaks inactive juice, for there is no penalty. Sometimes, however, as in a case of mine, *active* juice will cause a fatal fat necrosis, and I have wondered whether certain deaths reported as from " peritonitis " might not be due to that chemical misfortune.

AN EFFECT ON THE DIAPHRAGM OF REMOVING LARGE SPLEENS

The percentage of patients who died before they left Kasr el Aini Hospital after splenic resection was about 10 during my eleven years in Cairo. Apart from a very few accidents due to slipping of ligatures, and rare events like pancreatitis, acute gastric dilatation, or septic infection, this mortality was from complications affecting the lungs—pulmonary collapse and basal pneumonia being the chief causes of death.*

I had many opportunities of demonstrating, in the course of operation, derangements of the diaphragm after taking out large spleens. Blind clamping, of course, will bruise or tear, but much more interesting is the way in which the function of the diaphragm can suffer from relaxation caused by loss of the cushion on which it has long been moulded and stretched. I have witnessed three degrees of this relaxation in the left cupola: the first and least, a shallow wrinkling that soon vanished; second, the transverse folding of the diaphragm into ridges tall enough to grasp between finger and thumb, sometimes flattening out as contractility returned, but rarely quite gone before closing the belly. Last and less frequently, the whole left cupola became a slack, passive membrane, which, instead of descending with inspiration as the diaphragm should, rose into the thorax, and came down with each expiratory act. I only once saw the cupola recover during operation from this complete reversal of its movement.

It is likely that these effects of withdrawing a tense and perfectly moulded support from the diaphragm, so plainly seen in the left cupola, may well be matched in some degree by hidden changes in the right; for when the spleen is out the liver often moves over and partly occupies the empty bed.†

The support of *both* sides of the diaphragm must then be altered, and one may suppose that derangements of phrenic function, caused by consequent crumpling and looseness, might then cripple the base of *either* lung and favour collapse and possible pneumonia.

I was well aware that chest complications did not always follow observed relaxation of the diaphragm, for this is only one of several factors that help to collapse

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* An unusual *non*-fatal complication in a boy aged 15 was volvulus of the whole small gut. It occurred on the eighth day after removing a huge spleen. I reopened the wound and untwisted the mesentery. Recovery was smooth.

† In one of my cases at the British Postgraduate Medical School the shift was so complete that the left hepatic lobe covered the *whole* summit of the left cupola. (Failing the liver, intestines as a rule migrate into the spleen-bed unless the stomach happens to be distended.)

and menace the lung. It was, however, desirable to find means of avoiding contributory effects due to gross change in the movements of respiration, and guidance came from those cases where cupolas, after a flickering pause, smoothed their wrinkles and went to work. These, and especially the single case of complete flaccidity recovering tone during operation and developing no chest complications afterwards, seemed to promise that if only we could help the diaphragm quickly to win back its lost tension, all might yet be better if not absolutely well.

I therefore left, in place of the spleen, a child's balloon. At the suggestion of my then theatre sister, Miss Rawel, an oxygen cylinder was used to inflate it through sterile tubing, and this was clamped when the balloon filled the cupola. Nothing endures, however; balloons wilt and the gloss goes, but now—at last—this source

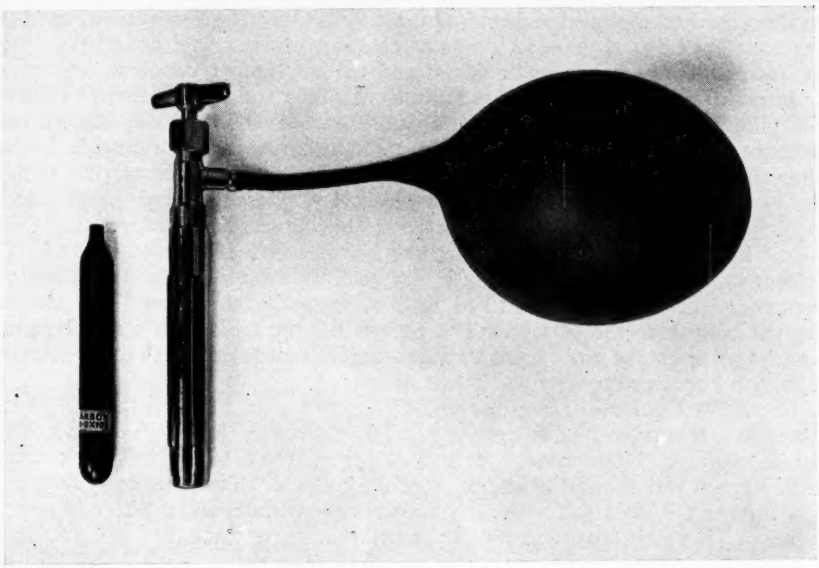

FIG. 342.—Rubber balloon attached to Sparklet resuscitator and partly inflated with CO_2. (A spare bulb is shown.) The balloon is designed to counteract the effects of relaxation of the diaphragm caused by suddenly removing the support of a large spleen. The long tubular process projects through the abdominal wall for inflation or deflation.

of nursery tears was harnessed to good purpose, for the slow shrinking gave the diaphragm time to tune its fibres to the fall of tension.

My span in Egypt was then nearing completion so that I had the opportunity of inserting these toy balloons in only 6 cases. Four I am convinced were benefited, and experienced sisters who nursed them noticed that, unlike other cases, they could easily cough and bring up sputum in the first few hours after splenectomy. This would seem valuable, for the sputum ejected was thick and of the kind that blocks bronchioles and favours pulmonary collapse. We noticed that respiration in those patients with balloons was more rapid immediately after operation than in those without, the increased rate falling when we withdrew them on the third or fourth post-operative day. By that time a balloon was sufficiently deflated to come out easily, and it was interesting to see impressions left on it by large intestine; a gush of clear fluid accompanied removal whether ascites had previously been present or not. In the fifth case the balloon broke quietly without damage to the patient.

The sixth died in a brief outbreak of sepsis that swept the hospital impartially during demolition of old wards, and I did not then feel justified in exposing other patients to a risk from foreign bodies while dust fell. Meantime, however, I asked Messrs. Thackray to make me balloons less fragile than our toy models, and on their advice obtained a 'sparklet' resuscitator with bulbs of carbon dioxide—a light compact apparatus easily sterilized and excellent for gentle inflation (*Fig.* 342). Unfortunately these promising things arrived close on my return to England and were not used.

I append in conclusion a record, most kindly found for me at Kasr el Aini by Dr. Bayumi Bey, F.R.C.S., describing the only difficult operation in which I used a balloon. I have added some careful notes made at the time by Dr. Abdalla Magdi.

Case No. 7308: Egyptian splenomegaly. Male aged 30. Year, 1935. Kasr el Aini Hospital, Cairo.—

The spleen reached the navel and crossed the middle line; the liver was enlarged and firm.

OPERATION (June 19, 1935).—This was carried out under spinal anæsthesia (5 per cent novocain) injected between the 12th dorsal and the 1st lumbar vertebræ, accompanied by ephedrine intravenously. No ascites was found. Multiple and dense adhesions were present between diaphragm and spleen, and the case would have been inoperable without the use of the high-frequency current. Even the current did not prevent considerable hæmorrhage, and an hour after the operation began systolic pressure had fallen from 130 to 68 mm. About 300 c.c. of blood were baled from the abdominal cavity, filtered through gauze into a Denis Browne syringe, and there citrated for intravenous injection. Systolic pressure quickly rose to 100 mm. Ten minutes before closing the abdomen a balloon, placed in the bed vacated by the spleen, was gradually distended with oxygen till it supported the whole left cupola of the diaphragm. The abdomen was filled with saline and closed round the clamped tube connecting the balloon to the surface. The patient left the table with a systolic pressure of 110 mm. and a pulse-rate of 90. Nitrous oxide was given during the final thirty minutes of the operation, which lasted exactly one and a half hours.

POST-OPERATIVE COURSE.—The pulse and respiratory rates rose, on the day of operation and the day after, to 140 and 54 respectively. The patient *in the first few hours* coughed up thick greenish sputum. Respirations averaged 40 per minute till the third post-operative day, when a little oxygen was allowed to escape from the balloon. The *respiratory rate at once fell sharply*; a further fall occurred when the balloon was withdrawn, 8 hours later—72 hours after operation. Respirations averaged 28 from that time until the patient's discharge. Removal of the balloon was accompanied by a gush of clear fluid. On the 8th post-operative day the temperature rose suddenly to 102·2° F., but fell again to 100·4° F. next day and soon became normal. No increase in the rate of pulse or respiration accompanied the rise in temperature, though the patient complained of transient pain over both lung bases just after this rise. His condition on discharge was satisfactory.

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JEJUNOGASTRIC INTUSSUSCEPTION

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If a gastro-enterostomy has both an afferent and an efferent jejunal loop, three types of jejunogastric intussusception may occur as rare complications of the anastomosis :—

Type I.—The afferent loop alone may intussuscept through into the stomach.

Type II.—The efferent loop may undergo retrograde intussusception and either stop short of, or pass through, the gastro-enterostomy stoma.

Type III.—Both afferent and efferent loops together may intussuscept through into the stomach.

The first case to be recorded was described by Von Steben[1] (1917) in Germany, while in this country Richard Warren[2] (1919), of the London Hospital, soon followed with a description of a case. Up to 1937, only 37 cases of jejunogastric intussusception had been described (Ducey and McNamara[3], 1937) and since then I have been able to find the records of a further 3 cases by Bonomi[4] (1937), Greenwood[5] (1937), and Otero[6] (1938), besides the case reported here, which is an example of Type III.

CASE REPORT

History.—E. J. W., male, dairyman, aged 68, was admitted to Hammersmith Hospital on February 13, 1939, with colicky abdominal pain and vomiting.

In April, 1936, a posterior no-loop gastro-enterostomy for pyloric stenosis had been done by Professor Grey Turner. Convalescence was normal. No vomiting or abdominal pain occurred until February 13, 1939, at 7.0 a.m., when while working, there was a sudden onset of severe abdominal pain in the epigastrium, colicky in nature. There was no radiation of pain, which eased somewhat by sitting up and bending forwards and by vomiting, which had occurred four times during the day. The vomit was brown in colour and, according to the patient, contained no red blood. The pain had increased in intensity during the day. The bowels were regular and had opened normally that day.

On Examination.—The patient looked poorly and preferred to sit up in bed, leaning well forwards. Extremities were somewhat cold. The pulse was of good volume, rate 84. Temperature, 98·8°. Respirations, 24. The abdomen showed poor movement on respiration and a well-healed firm upper abdominal midline scar. Tenderness and rigidity were present in the epigastrium and also down the right side of the abdomen. No distension or visible peristalsis was seen. Per rectum, no abnormality was discovered. The chest was normal.

It was thought that the patient either had a leaking duodenal ulcer or was suffering from a jejunogastric intussusception. Immediate operation was advised and agreed to by the patient. It was only when the anæsthetist reported that during induction of anæsthesia by gas–oxygen and ether the patient vomited some bright red blood, that the diagnosis of jejunogastric intussusception was made.

On the operating table the distended stomach was visible.

At Operation (15 hours after onset of pain).—A midline upper abdominal incision was made and some half-pint of turbid brown fluid was found in Morison's pouch. (Pathological report by Dr. Janet Vaughan showed red blood-corpuscles and leucocytes in the proportion found in blood. Fibrinous material, debris, and endothelial cells, 60 per cent polymorphs. Cultures sterile.)

The attachment of the greater omentum to the greater curve of the stomach was very œdematous. The stomach was large. The transverse colon was turned upwards and a

considerable amount of small bowel was seen to disappear up behind it as if through the gastro-enterostomy. The stoma was not visualized at this stage of the operation.

By pulling on the small bowel it was seen that it had intussuscepted through the stoma into the stomach, and it reduced easily to reveal about 2½ ft. of red congested jejunum. At this stage it was thought to be completely reduced, but a further 1 ft. was withdrawn which was red and congested, and distended to about twice its normal size.

The gastro-enterostomy stoma was then seen, and appeared normal apart from a hæmorrhagic area ½ × ½ in., due to extravasated blood following mechanical congestion, on the anterior surface of the anastomosis. No ulceration was seen or felt in the stomach, duodenum, or anastomosis. No attempt was made to anchor the jejunum.

CONVALESCENCE.—Some post-operative bronchitis, but patient was well and discharged on the nineteenth day.

FOLLOW-UP.—

March 7, 1939.—Barium meal (Dr. Duncan White). Stomach orthotonic. Peristalsis sluggish but present. For about ten minutes no barium was seen to reach the stoma, but then it passed through the gastro-enterostomy stoma. No filling defect or other abnormality seen.

In five hours the stomach was nearly empty and the head of the meal lay in the transverse colon.

COMMENTS.—Gastro-enterostomy functions well. No alimentary lesion now present.

March 11, 1939.—Attempt at gastroscopy failed because the patient was uncooperative.

Aetiology.—Von Steben (1917) described his original case occurring in a pregnant woman, and pregnancy has since been considered to be an aetiological factor. This is hardly justified in view of the fact that the majority of cases have been uncomplicated by pregnancy, and many have occurred in males.

Hamilton Drummond[7] (1923) suggested that the acid contents of the stomach on reaching the jejunum irritate it and cause antiperistalsis, and when the jejunum is intussuscepted through the stoma further portions of it are drawn in by the efforts of the stomach to eject its contents. If this were so we should expect many more cases to occur, perhaps as many as the cases of gastrojejunal ulceration. Furthermore, no case of associated anastomotic ulcer has been recorded (Adams[8], 1935).

In the majority of cases reported, especially those which reached post-mortem examinations, both afferent and efferent loops together had passed into the stomach. But since intussusception can occur singly in either the afferent—Ledoux-Lebard and Garcia Calderon[9] (1933) and Sibley[10] (1934)—or the efferent loop—Debenham[11] (1935) and Otero (1938)—it may well be that the cases in which both loops have intussuscepted through into the stomach have really begun in one or other jejunal loop and have progressed to the final condition. It should be emphasized, however, that if this theory is true, the process must be a rapidly progressing one, because almost all the reported patients with jejunogastric intussusception in which both afferent and efferent loops were together involved, had not suffered with previous symptoms.

The condition has never been described following gastro-enterostomy performed for carcinoma of the stomach (Adams, 1935), but since the majority of cases have occurred after eighteen months following gastro-enterostomy, and since we know only too well that a similar survival period after the same operation for cancer of the stomach is a rarity, the statement is not so surprising as it might at first appear. However, Drummond quoted a case described by Lundberg which was said to have occurred ten years after a gastric resection with gastro-enterostomy for a cancer of the stomach. At post-mortem no evidence of growth was found.

From an analysis of 33 cases reported in the literature up to 1933, Bettman and Baldwin[12] (1933) stated that the condition had occurred any time from a few days to several years after a gastro-enterostomy. It had occurred after both anterior and posterior gastro-enterostomy, with or without entero-anastomosis. The condition had also recurred. It had occurred in both males and females, and there was no obvious sex predomination.

Diagnosis.—The diagnosis becomes clear if the anatomy of the part is considered.

Type I (*Fig.* 343).—If the afferent loop alone is intussuscepted, postprandial upper abdominal pain with exacerbations of epigastric colic and bilious vomiting occur as a result of the subacute intestinal obstruction. The cause of these symptoms may be overlooked for some time, and repeated attacks, perhaps with intermissions corresponding to spontaneous reduction of the intussusception, may occur and will only be diagnosed if the patient is seen during an attack and either gastroscopy or radiological examination is performed at once.

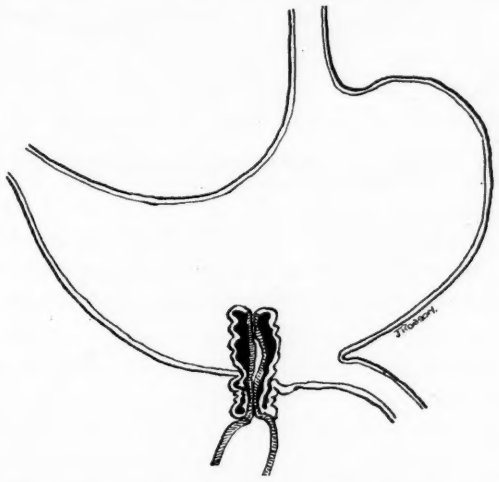

FIG. 343.—Type I. Intussusception of afferent loop.

The radiograph will show a distended afferent loop (or duodenum), and an opaque meal will outline a rounded filling defect in the stomach due to the intussusception and upon which will be seen the relief pattern due to the jejunal plicæ.

It is important to consider the possibility of such a condition in any case of so-called ' gastro-enterostomy dysfunction '. The incompleteness of the obstruction is due to the fact that the efferent loop still retains its function, and it is because of this that the term chronic has been applied to this type of jejunogastric intussusception.

Type II (*Fig.* 344).—If the efferent loop undergoes retrograde intussusception, then an acute high small-bowel obstruction results, and the typical symptoms of colicky abdominal pain with vomiting of gastric, bilious, and then intestinal contents follow.

Type III (*Fig.* 345).—Similarly if both afferent and efferent loops together intussuscept through into the stomach, acute high intestinal obstruction results and its typical symptoms will follow.

The misleading feature in many of the cases of jejunogastric intussusception seems to have been that the symptoms had been ascribed either to other possible complications of the gastro-enterostomy—e.g., stomal inflammation or ulceration—

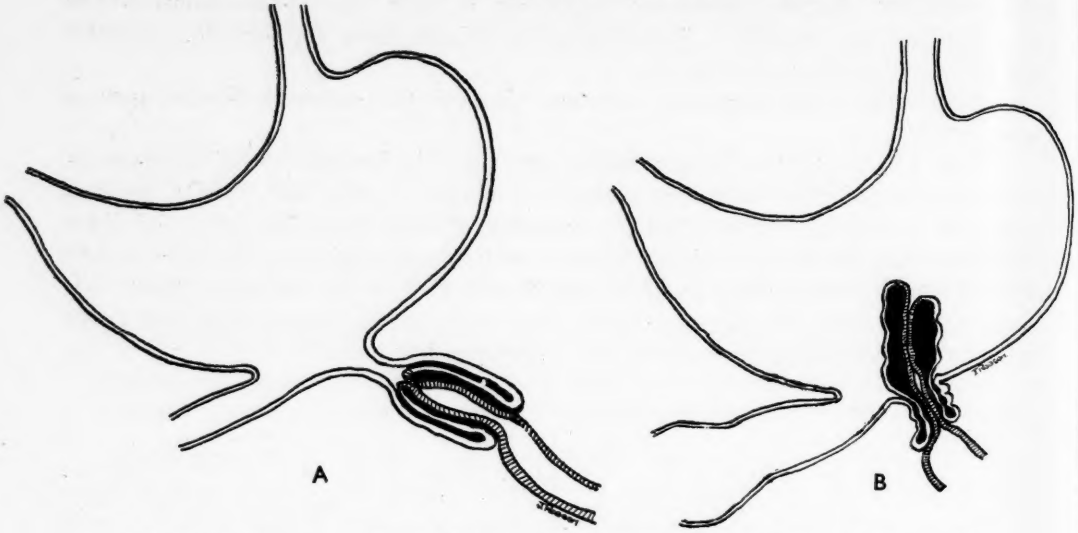

FIG. 344.—Type II. A, Retrograde intussusception stopping short of stoma; B, Retrograde intussusception passing through stoma.

or to complications of the condition for which the gastro-enterostomy had been performed—e.g., leaking perforation of an ulcer, or hæmatemesis from a bleeding ulcer. Just as in cases of intussusception of the lower ileum in children, in which

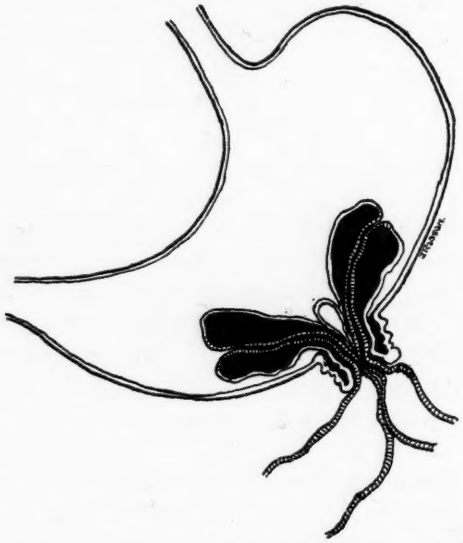

FIG. 345.—Type III. Intussusception of both afferent and efferent loops.

the bowel becomes mechanically compressed and congested, blood is extravasated into its lumen, and may be ejected from its orifices, so also may the same process occur in jejunogastric intussusception, and consequently it is not surprising that

hæmatemesis often occurs. If the possibility of the origin of the blood is overlooked, the case may be treated as a medical emergency, e.g., hæmatemesis, and either operation delayed until it is too late or else the correct diagnosis only made at autopsy. That this may be the case is emphasized by the fact that in almost 30 per cent of the cases recorded it was the post-mortem examination which first revealed the true diagnosis.

Treatment.—In all types of jejunogastric intussusception, surgical treatment is necessary.

In Type I, in which only the afferent loop is intussuscepted and the symptoms are recurring, reduction by gentle traction should be performed and recurrence prevented by one of several procedures—the afferent loop can be anchored by sutures to either the stomach or the transverve mesocolon ; the gastro-enterostomy can be undone ; or a partial gastrectomy including resection of the anastomosis may be deemed necessary.

In Type II, where the efferent loop has undergone retrograde intussusception, simple reduction by traction will suffice, but if operation is delayed and the loop is gangrenous, resection will be necessary.

In Type III, when both afferent and efferent loops are together involved, if the operation is undertaken early, reduction by traction is likely to be successful, but the stoma must be visualized to be sure that all the intussusception has been reduced.

Although it is true that recurrences have occurred, and that as such some attempt might be made to prevent this happening by stitching the afferent and efferent loops of jejunum together, cases of intussusception have occurred where an entero-anastomosis has been carried out at the time of the gastro-enterostomy, and so it would hardly seem justifiable. Just as most surgeons are satisfied to reduce an ileocæcal intussusception without fixing the bowel, so with cases of jejunogastric intussusception in which both afferent and efferent loops together are involved. The best safeguard if recurrence does occur is usually the patient. He, or she, will know what has happened, and in fact, up to 1933, when Bettman and Baldwin reviewed 33 cases, although a correct pre-operative diagnosis had been made in only three cases, in two of these, because they were recurrences, the patients themselves were able to make the correct pre-operative diagnosis.

If operation is undertaken at a late stage, and simple reduction is impossible, it may be necessary to incise the stomach down to, and including, the gastro-enterostomy stoma, and after freeing the jejunum, to suture the gastrotomy. If the jejunum is gangrenous, then a resection and anastomosis will be necessary, but as the resection would be very close to the gastro-enterostomy it is likely to be extremely difficult to perform, and would necessarily carry a high mortality. I believe it would be safer to pass a series of Lembert sutures through the intussuscepting jejunal loops and the stomach, and between the afferent and efferent loops of jejunum, and then to amputate the prolapsing intragastric jejunal loops through a gastrostomy.

The usual post-operative resuscitative measures such as salines and blood transfusions must be given whenever necessary.

Prognosis.—So few cases of Type I, in which only the afferent jejunal loop is involved, have been recorded (I can only find the records of 6 cases), that to venture an opinion on the prognosis would be valueless. However, although it will depend on early accurate diagnosis, it will depend chiefly on surgical technique. If a resection

is performed, the mortality will increase proportionately to the severity of the operation undertaken.

The prognosis of the Types II and III depend more on early diagnosis. Ducey and McNamara (1937) analysed the cases in the literature, and out of 37 cases recorded, 28 were submitted to laparotomy, and of these only 19 recovered. Since then I have been able to find the records of a further 2 cases of these types, 1 fatal (Greenwood, 1937) and 1 successfully treated (Otero, 1938), so that a mortality of 50 per cent is apparent. If early operation is carried out, the prognosis is good, and of 15 patients operated on within forty-eight hours of onset, all recovered, whereas of 10 patients operated on after forty-eight hours, there was a mortality of 50 per cent (Bettman and Baldwin, 1933).

SUMMARY

Jejunogastric intussusception is a rare complication of gastro-enterostomy.

Three types are described: Type I, afferent loop alone; Type II, efferent loop alone; Type III, both afferent and efferent loops.

A further case (Type III) is reported in which the correct pre-operative diagnosis was made.

The aetiology of the condition is obscure.

The condition should be considered if ever a patient has abdominal pain and vomiting, with or without hæmatemesis, coming on at any time after a gastro-enterostomy.

The treatment is surgical.

In Types II and III there is a 50 per cent mortality if operation is delayed more than forty-eight hours after onset of symptoms.

I express my thanks to Sir Frederick Menzies for permission to publish the case record, and to Professor Grey Turner and Professor A. K. Henry for help and advice.

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DISLOCATION OF THE INFERIOR RADIO-ULNAR JOINT AS A COMPLICATION OF FRACTURE OF THE RADIUS

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FRACTURES of the radius are not uncommonly complicated by dislocation of the inferior radio-ulnar joint; in our experience a combination of the two forms quite an appreciable percentage of arm injuries. Dislocations of the inferior radio-ulnar joint forming a component of a severe Colles's fracture are common and well recognized; the other types are inadequately described in current literature.

In 1912 Darrach[1] published 2 recent cases of anterior dislocation of the head of the ulna following trauma, in both of which an open operation was necessary. Gibson[2] in 1925 gave an account of uncomplicated dislocations of the head of the ulna, 35 of which had been described up to that time in the literature, and he added a further case of his own. In this paper he classified dislocations of the head of the ulna, and discussed the anatomy of the wrist with regard to such cases. Galeazzi[3] in 1935 discussed minutely the possible aetiological factors and mechanics of posterior dislocation of the lower end of the ulna together with fracture of the shaft of the radius, and stated that many of his forearm injuries were in this category; he gave, however, no detailed account of individual cases. In 1936 Gautier[4] mentioned a case of posterior dislocation of the head of the ulna associated with a fracture of the shaft of the radius, and pointed out the relative frequency of the syndrome, but no figures were quoted. Taylor and Parsons,[5] in 1938, emphasized the importance of the inferior radio-ulnar joint in Colles's fracture, and suggested a method of treatment in cases where this joint was disorganized. In view of the relatively frequent occurrence of the lesion, we feel the following account is justified, because many important points in the aetiology, pathology, mechanics, and prognosis have not hitherto been described.

Dislocations of the inferior radio-ulnar joint occurring as a late complication of an injury to the forearm (a traumatic Madelung's deformity) will not enter into the scope of this article, as they receive sufficient mention in the literature.

Definition.—The distinction between a subluxation and a true dislocation of the inferior radio-ulnar joint is often difficult to assess clinically, because of the relatively small dimensions of the opposed articular surfaces. Dislocation of the inferior radio-ulnar joint is present when there is complete separation of the head of the ulna from the articular surface of the radius, as seen on a lateral radiograph of the wrist. Dislocation of the head of the ulna is anterior or posterior, and some distal displacement occurs in most cases.

FREQUENCY AND CLASSIFICATION

During the last two years 2684 patients with injuries of the upper extremity have been treated at the fracture clinic at the General Infirmary at Leeds; of these

1029 sustained wrist injuries and 540 had fractures of the forearm. We include greenstick fractures of the lower end of the radius and lesions of the carpal bones in our group of wrist injuries.

In this series 25 patients sustained injuries including dislocations of the head of the ulna, which can be classified as follows :—

Group I.—Anterior dislocation of the head of the ulna as a component of a severe Colles's fracture.

In defining what we mean by a severe Colles's fracture, the following factors are taken into consideration: (1) The degree of displacement and comminution of the lower end of the radius, especially where the radial articular surface is disorganized; (2) The length of attendance at the fracture clinic after removal of the plaster; (3) The end-result as regards function of the wrist and economic value of the hand.

In 602 Colles's fractures 135 were severe; 15 (11 per cent) of the severe fractures were complicated by a dislocation of the head of the ulna. It is likely, however, that the incidence was considerably higher, as a radiograph was not taken prior to manipulation in every case.

Group II.—Posterior dislocation of the head of the ulna associated with: (*a*) fracture of the shaft of the radius (6 cases); (*b*) fracture of the lower inch of the radius (2 cases).

Group III.—Anterior dislocation of the head of the ulna with fracture of the shaft of the radius (2 cases).

MECHANICS

In a general consideration of the mechanics of dislocation of the head of the ulna, the following facts concerning the anatomy of the wrist are important. The head of the ulna is relatively unstable when compared with the lower end of the radius, and it does not articulate with the carpus. The ulnar collateral ligament and the ligaments of the inferior radio-ulnar joint are not strong enough to prevent a certain amount of antero-posterior movement of the head of the ulna in the normal subject. In addition, there are no strong muscles or tendons in the region of the wrist to act as stabilizing factors of the joint. In spite of slight antero-posterior movement, the radio-carpal joint is stable because the opposing articular surfaces are closely adapted to each other and the radio-carpal ligaments are strong. From these facts it will be clear that when the wrist is subjected to trauma, dislocation of the head of the ulna is possible, whereas a similar displacement of the lower end of the radius is highly improbable.

As a rule a dislocation of the head of the ulna takes place in a direction opposite to that of the original violence. The lower radial fragment bears the brunt of the force and is avulsed from its attachments to the ulna, which remains, as it were, in situ; the dislocation of the head of the ulna so produced is thus entirely passive. The hand accompanies the distal radial fragment in the direction of the force, the radio-carpal ligaments being undamaged. This point is emphasized by Gibson,[2] who states :—

> The lesion is generally referred to as a dislocation of the head of the ulna. This is really a mistake in terminology. It is the ulna which remains fixed; it is the lower extremity of the radius which undergoes displacement. But not only is the lower end of the radius more massive than the lower end of the ulna; it carries with it also the whole carpus and the hand, so that it appears as if the ulna had undergone the displacement noted. Hence it is customary, although inexact, to accept the erroneous designation.

Dislocations in all groups are caused by severe violence in the region of the wrist (e.g., cases M. A., B. H., D. B., H. H.).

From the above considerations the sequence of events in these cases is as follows: After the impact of the blow in the region of the wrist the shaft of the radius breaks, angulates, and overlaps, thus causing shortening of the radial side of the forearm. The equivalent degree of shortening must also take place on the ulnar side; and because the humero-ulnar articulation is relatively more stable than the inferior radio-ulnar joint, dislocation of the head of the ulna then takes place. Some distal dislocation of the head of the ulna on the radius also occurs in most of the cases.

Mechanical factors affecting each group are as follows:—

Group I.—The lesion is produced by a fall on the outstretched hand, as in all Colles's fractures. The radius breaks in its distal inch and the distal fragment is forced posteriorly and proximally. The ulna dislocates anteriorly.

Group II.—The nature of the trauma in this group would appear to be the same in both subdivisions—namely, a heavy blow or fall on the posterior surface of the wrist or hand forcing the latter into extreme palmar flexion. In this group the site of fracture of the radius probably depends upon the angle of incidence of the forearm with the ground or opposing force, as suggested by Chiene[6] with reference to Colles's fractures.

The age of the patient may also be relevant in determining the site of the fracture. In our series, fractures involving the lowest inch of the radius appear only to occur at an age when the epiphyses are still present, the lesion being a fracture-separation of the lower radial epiphysis; but a definite conclusion cannot be drawn on such a small number of cases.

Galeazzi compared cases in this group with Monteggia's syndrome of fracture of the upper third of the shaft of the ulna associated with an anterior dislocation of the head of the radius. He stated that the obliquity of the stress from the distal end of the radius to the proximal end of the ulna, following a fall on the abducted outstretched hand, may cause either lesion. In our experience, however, the nature of the violence in such cases has been a blow on the palmar-flexed and not on the outstretched hand. Incidentally we have also got examples of cases where Monteggia's syndrome occurred following direct violence in the region of the elbow.

In children fractures of the lower third of the radius are not complicated by a dislocation of the head of the ulna even when there is gross angulation and shortening of the radius. The probable explanation is that in such cases the ligaments are lax as compared with adults and can thus accommodate the necessary degree of shortening of the forearm without allowing a dislocation to occur.

Group III.—The mode of injury in these cases is similar to that of a Colles's fracture—namely, a fall on the outstretched hand, resulting in an anterior dislocation of the head of the ulna and a fracture of the shaft of the radius.

PATHOLOGICAL ANATOMY

Several points which might have been included under this heading have already been mentioned above; the remaining details which are of importance can be tabulated as follows:—

1. Disorganization of the inferior radio-ulnar joint always takes place; it is most commonly due to a rupture of the triangular fibrocartilage. However, as

Taylor and Parsons[5] point out, avulsion of the ulnar styloid process at its base, or fracture of the radius at the insertion of the fibrocartilage, may sometimes result in the same disorganization.

2. In all cases rupture of the ulnar collateral ligament or fracture of the tip of the styloid process of the ulna must occur. Of our 25 cases 10 sustained a fracture of the ulnar styloid process.

3. The radio-carpal ligaments are uninjured; thus palmar flexion and dorsiflexion of the hand are usually little impaired. Where the fracture involves the radial articular surface, as may occur in Group I, these movements may be adversely affected.

CASE REPORTS

Group II (*a*).—

Case 1.—A. W., male, aged 41. Occupation, labourer.

HISTORY.—On July 6, 1938, he received a blow on the dorsum of the right wrist by a crane weighing over a ton.

ON EXAMINATION.—The shaft of the radius was fractured at the junction of the middle and lower third, and the head of the ulna was dislocated posteriorly, the ulnar styloid process being broken.

TREATMENT.—Under gas and oxygen anæsthesia the arm was manipulated and plaster-of-Paris applied to the elbow, forearm, and wrist, which was fixed in dorsiflexion. A further radiograph showed that reduction had been obtained.

AFTER-TREATMENT.—Finger movements were full and swelling of the hand had gone nine days after manipulation. The plaster was removed on August 24, 1938, when the fracture was found to be firm. A triangular sling was applied for a week. In the middle of September there was some pain over the site of the fracture, but a new radiograph showed solid bony union of the radius. Movements and function of the wrist gradually improved until the patient was discharged on December 15, 1938. On this date the end-result was as follows: Elbow movements were full; at the wrist dorsiflexion, palmar flexion, and pronation were full; supination was three-quarters of normal range; the grip was good. Light work had been started at the end of October, and on discharge the patient had been doing full work for some weeks, though he said that heavy lifting (2 cwt.) was not so easily performed as prior to the injury.

FIG. 346.—*Case* 2. Posterior dislocation of the head of the ulna with fracture of the shaft of the radius; antero-posterior view. Before manipulation.

Case 2.—S. B., a nun, aged about 30.

HISTORY.—On June 24, 1938, the patient sustained a fall from a ladder on to the back of her right hand, which was violently palmar-flexed.

ON EXAMINATION.—The shaft of the radius was broken in its lower third and the head of the ulna was dislocated posteriorly (*Fig.* 346).

TREATMENT.—Under gas and oxygen anæsthesia, the arm was manipulated and plaster-of-Paris applied as in *Case* 1. A further radiograph showed incomplete reduction of the dislocation and some anterior angulation of the radius. Re-manipulation and plaster resulted in complete reduction.

AFTER-TREATMENT.—Finger movements were full in three days and the plaster was removed on August 10, when the fracture was firm. Active use of the arm was started after one week in a sling. On September 30 all movements were full except for some slight limitation of supination, which was still present when the patient was

discharged at the end of November. Work was resumed within three weeks of the removal of the plaster.

Case 3.—D. B., male, aged 42. Occupation, labourer.

HISTORY.—Severe blow on the dorsum of the left wrist on August 19, 1938.

ON EXAMINATION.—Radiograph showed an oblique fracture of the lowest quarter of the radius and a posterior dislocation of the lower end of the ulna, with fractured ulnar styloid; there was also an ununited fracture of the carpal scaphoid dating from an injury several years previously (*Fig.* 347).

TREATMENT.—Under gas and oxygen anæsthesia the arm was manipulated and plaster-of-Paris applied as in *Case* 1. A further radiograph showed full reduction (*Fig.* 348).

AFTER-TREATMENT.—Swelling of the hand was severe enough to necessitate re-plaster three days after reduction. The following day finger movements were full, and a further radiograph showed the reduction had been maintained The plaster was removed on September 12, when the fracture was firm and active use of the arm was started. The patient was last seen on December 8 when all movements of the wrist were full; there was, however, some pain on pressure over the ulnar collateral ligament. The patient had been doing full work since the beginning of November, 1938. The patient received no treatment for the ununited fracture of the scaphoid.

Case 4.—M. A., female, aged 36. Occupation, typist.

HISTORY AND EXAMINATION.—On February 19, 1938, as a result of a motor-car accident, the patient was admitted to a general surgical ward suffering from multiple injuries. One of these subsequently was proved to be a posterior dislocation of the head of the right ulna (*Fig.* 349).

TREATMENT.—Two days after admission the wrist was manipulated under general anæsthesia and plaster-of-Paris applied to the forearm and wrist as in *Case* 1. A further radiograph showed the presence of a fracture of the shaft of the radius which had not been diagnosed and was unreduced. Re-manipulation and the application of plaster-of-Paris to the wrist, forearm, and elbow resulted in satisfactory reduction. (*Fig.* 350).

AFTER-TREATMENT AND PROGRESS.—Full range of finger movements was regained in three days after the second plaster. On April 21 the plaster was removed, and when the patient was discharged on November 23 all the movements were full apart from slight limitation of supination. The patient had been doing full work from June, 1938.

Case 5.—J. M., male, aged 25. Occupation, labourer.

HISTORY.—On December 8, 1938, an accident at work resulted in a fracture of the middle of the shaft of the right radius. The radiograph showed no displacement of the fragments.

TREATMENT.—Plaster was applied to the elbow, forearm, and wrist; there was a full range of finger movements a week after the injury.

AFTER-TREATMENT AND PROGRESS.—The plaster was removed six weeks after the injury, when the fracture was found to be firm clinically. The patient was seen twice during the succeeding four weeks, at the end of which time there was found to be some posterior angulation at the site of the fracture and subluxation of the head of the ulna. A new radiograph showed bony union to be occurring, but not yet complete. A new plaster was applied and the patient is still under treatment. The subluxation of the head of the ulna was not evident when the patient was first seen, but its subsequent appearance was presumably due to the combined effect of injury to the ligaments at the lower end of the ulna at the time of the accident and the angulation of the shaft of the radius, noted above.

Case 6.—K. L., male, aged about 26. Occupation, labourer.

This was an untreated case. The patient attended the General Infirmary at Leeds for a cut finger, when gross deformity in the region of the right wrist was noticed. It proved to be due to a posterior dislocation of the head of the ulna and there was some angulation of the shaft of the radius. The patient said that he had fractured his arm ten years previously and that it had been found to be impossible to reduce the dislocation at that time. The function of the hand was remarkably good when seen; there was full range of palmar flexion, three-quarters range of dorsiflexion, and rotation was limited by half. The grip was good and the patient was doing full work as a labourer.

FIG. 347.—*Case* 3. Posterior dislocation of the head of the ulna with fracture of the lower quarter of the shaft of the radius. Before manipulation.

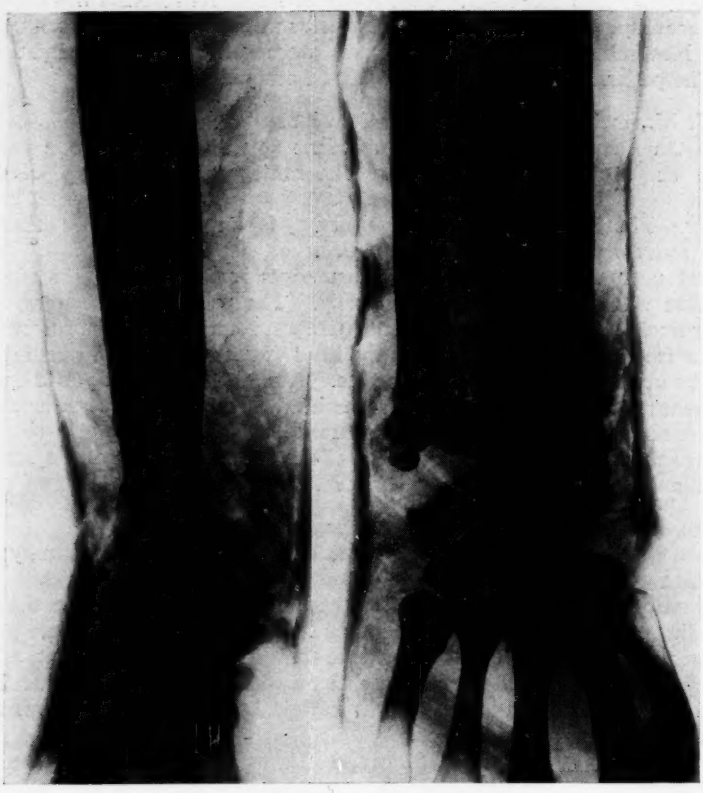

FIG. 348.—*Case* 3. After manipulation.

FIG. 349.—*Case* 4. Posterior dislocation of the head of the ulna with fracture of the shaft of the radius. Before reduction. The only case clearly showing dislocation of ulna from radius.

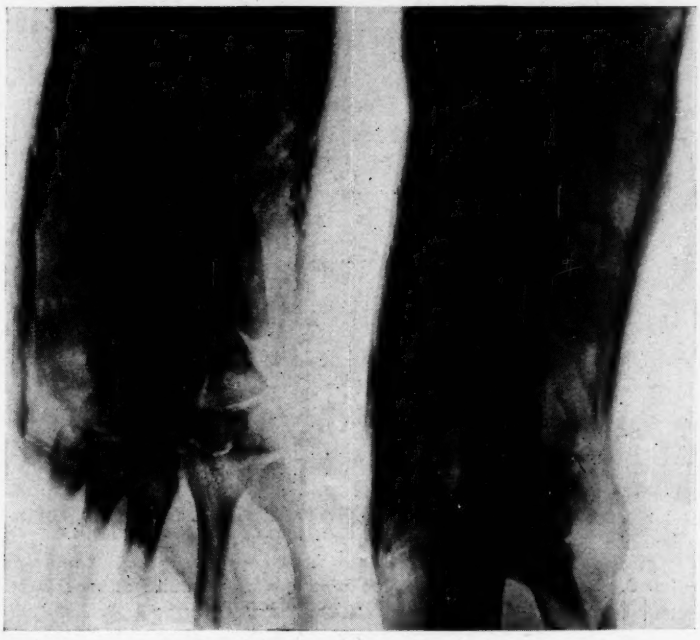

FIG. 350.—*Case* 4. After manipulation.

Group II (*b*).—

Case 7.—A. W., male, aged 15. Occupation, tailor.

HISTORY.—On August 15, 1938, the patient fell from his bicycle, causing violent palmar flexion of his left wrist.

ON EXAMINATION.—Radiograph showed an anterior fracture-separation of the lower radial epiphysis with a posterior dislocation of the head of the ulna.

TREATMENT.—Under gas and oxygen anæsthesia the wrist was manipulated and plaster applied to the forearm and wrist, the latter being fixed in dorsiflexion. A further radiograph showed reduction of the dislocation and fracture.

AFTER-TREATMENT AND PROGRESS.—Finger movements were full in two days. The plaster was removed four weeks later, after which the patient defaulted. He was asked to attend on February 10, 1939, when examination showed that all movements were full. The only abnormal physical sign was a click on antero-posterior movement of the ulna on the radius; this movement was painless. Full work had been resumed a few days after removal of the plaster.

Case 8.—B. H., male, aged 17. Occupation, labourer.

HISTORY.—The fingers of the patient's right hand were caught in the cogs of a machine on August 29, 1938. This accident resulted in a traumatic amputation of the middle finger and violent palmar flexion of the wrist-joint.

ON EXAMINATION.—A radiograph showed an anterior fracture-separation of the lower radial epiphysis and a posterior dislocation of the head of the ulna. The ulnar styloid process was also fractured (*Fig.* 351).

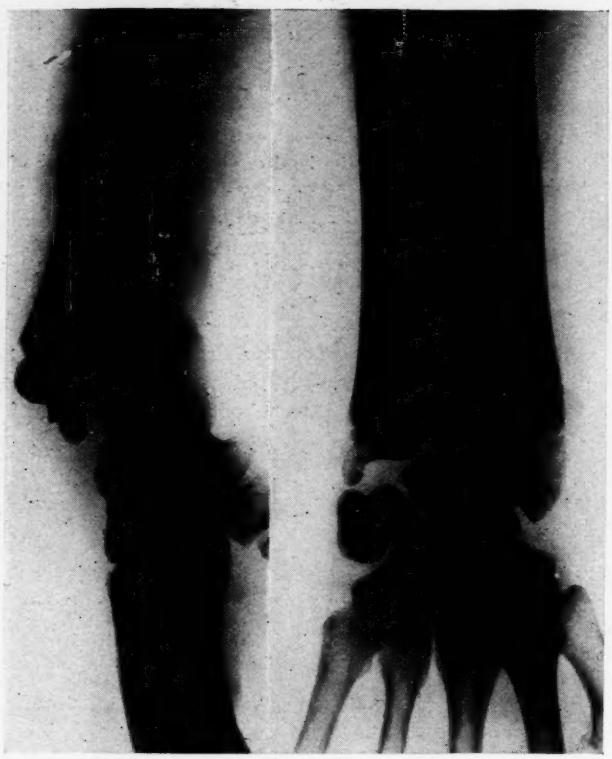

FIG. 351.—*Case* 8. Posterior dislocation of the head of the ulna with fracture-separation of the lower radial epiphysis. Before manipulation.

TREATMENT.—Under gas and oxygen anæsthesia toilet and re-amputation of the finger were performed and the wrist was manipulated; plaster was applied to the forearm and wrist, the latter being fixed in dorsiflexion. A new radiograph showed reduction of the fracture and dislocation.

AFTER-TREATMENT AND PROGRESS.—Finger movements were full in four days. The plaster was removed six weeks later, and when the patient was discharged on October 26 all movements were full, apart from slight limitation of supination. Work had already been resumed.

Group III.—

Case 9.—S. W., male, aged 78, an old-age pensioner.

HISTORY.—On January 14, 1939, the patient fell down some steps on to the outstretched left hand.

ON EXAMINATION.—There was a fracture of the shaft of the radius at the junction of the middle and lower thirds, with an anterior dislocation of the head of the ulna. The fracture of the radius showed marked anterior angulation of the bone and half an inch of overlap (*Fig.* 352).

TREATMENT.—Under gas and oxygen anæsthesia the arm was manipulated and plaster-of-Paris applied to the elbow, forearm, and wrist. A further radiograph showed reduction of the dislocation and also of the shortening and angulation of the radius; there was, however, no apposition of the fragments. In a younger man a further manipulation would have been performed, but in view of the age and general condition of the patient such manipulation was thought to be unwise.

AFTER-TREATMENT AND PROGRESS.—The patient's arm is still in plaster at the time of writing; finger movements were full four days after application of the plaster.

FIG. 352.—*Case* 9. Anterior dislocation of the head of the ulna with fracture of the shaft of the radius. Before manipulation.

Case 10.—A. D., male, aged 18. Occupation, bricklayer.

HISTORY.—On August 23, 1938, he fell on the outstretched left hand.

ON EXAMINATION.—A radiograph showed a fracture of the lower third of the shaft of the radius, with anterior dislocation of the head of the ulna. There was a small puncture wound on the anterior aspect of the wrist.

TREATMENT.—Under general anæsthesia the wound was excised and sutured; the wrist was manipulated and plaster-of-Paris applied to the forearm, wrist, and elbow. A further radiograph showed reduction of the fracture and dislocation.

AFTER-TREATMENT AND PROGRESS.—Finger movements were full six days later and the plaster was removed after a period of six weeks. The patient was discharged on October 6, when all movements were full apart from supination, which was three-quarters of normal range. The patient resumed his full work immediately after his discharge.

CLINICAL DIAGNOSIS

Dislocation of the inferior radio-ulnar joint may be suspected on observation of the following points:—

Group I.—

1. There is loss of the usual dorsal prominence of the head of the ulna, though this may also occur in fractures of the lower end of the radius where there is severe posterior displacement and angulation of the lower fragment unassociated with a dislocation of the ulna.

2. The head of the ulna may present as a prominence on the anterior aspect of the wrist.

3. There may be abnormal mobility of the head of the ulna on the radius in an antero-posterior plane. The elicitation of this sign may be impracticable because of pain.

Group II.—

1. The prominence of the head of the ulna on the posterior aspect of the wrist is accentuated.

2. The abnormal mobility, noted above, may be present.

3. Concentration on the gross deformity of the wrist may cause the fracture of the shaft of the radius to be overlooked, particularly when it is situated in the middle third of the bone—as actually happened in one of our cases (*Case* 4).

4. Posterior angulation of the shaft of the radius may be demonstrable clinically.

Group III.—The diagnosis was made on radiological examination.

PROGNOSIS

In spite of the severity of the lesion the prognosis in Groups II and III is remarkably good. As will be seen from the account of the cases given above, all the patients returned to their full work. The average disability period was between eight and ten weeks.

Though Galeazzi[3] reported a tendency to instability of the inferior radio-ulnar joint, we have only one case where this has occurred (*Case* 5); it is significant that this was the only case where there was angulation of the shaft of the radius at the conclusion of treatment, and it would therefore appear that it is of great importance to correct this displacement.

Even when the dislocation of the head of the ulna remains unreduced, the function of the wrist may be very good, as happened in one of our cases noted above (*Case* 6).

Limitation of supination occurs in many of the cases; but when the severity of the lesion is considered, it is surprising that this limitation is of so small a degree, and economically the results have been satisfactory.

The outlook in Group I, however, is not so hopeful. The average disability period was 14–16 weeks in those cases where the carpal articular surface of the radius was involved by the fracture; the longest time before discharge was 20 weeks, the shortest 6 weeks. The end-result was functionally good in only 6 cases, fair in 5, and poor in 1 case. Where the articular surface of the radius was not involved by the fracture, the average disability period was 6–7 weeks, and the end-result was good in 1 case and fair in 2 cases. Rotation of the forearm was limited to a more or less marked degree in all the cases in Group I.

Explanation of the poor prognosis in this group is probably as follows:—

1. The average age of the patients was 55 years, as compared with 29 in the other groups, and it is well known that injuries to joints in older people have not such a good prognosis as in younger people.

2. Limited dorsiflexion and palmar flexion of the wrist in these cases can be accounted for by the frequent involvement of the radial articular surface by the fracture.

3. Patients in this group were not treated by the method described by Taylor and Parsons[5] and by Mayer,[7] who advocate inclusion of the elbow as well

as the wrist in plaster and stress the importance of immobilizing the wrist for a period in a position of palmar flexion with extreme pronation and ulnar adduction. The limitation of rotation in our cases might have been prevented to a large extent if we had adopted this method.

TREATMENT

Immediate Treatment.—No special difficulty was encountered in treating these injuries. Under gas and oxygen anæsthesia satisfactory reduction following manipulation and plaster was obtained. In 25 cases a second manipulation was found to be necessary in only 4. Where the dislocation of the head of the ulna was anterior, the wrist was fixed in palmar flexion; where the dislocation was posterior, the wrist was fixed in dorsiflexion. The plaster was applied to the forearm and wrist in all cases, and was only extended above the elbow when the shaft of the radius was broken. The forearm was immobilized in a position midway between pronation and supination, excepting in those cases complicating Colles's fracture, where a position of full pronation and ulnar adduction was adopted. In no case was an open operation necessary.

After-treatment.—The usual emphasis was laid on the active use of the fingers, shoulder, and elbow, where the last was not immobilized. The patients attended the fracture clinic daily until such movements were full. Plaster was retained for periods of from four to eight weeks; with the exception of *Case* 8, only in those cases where the shaft of the radius was broken was the plaster retained for more than four weeks.

Following removal of the plaster all active movements were begun, a sling being worn for one or two weeks in cases where the shaft of the radius was involved. No case of non-union occurred in this series. Special massage was only required in 2 cases in Group I and 1 case in Group II.

SUMMARY

Twenty-five cases of dislocation of the inferior radio-ulnar joint are described, 10 in detail.

A classification is given, and the aetiology, mechanics, and pathological anatomy of the lesion are discussed.

The prognosis and treatment are described.

We wish to express our thanks to Mr. R. Broomhead for allowing us to publish accounts of the above cases, which have been under his care.

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THE AETIOLOGY OF HALLUX RIGIDUS

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Describing hallux rigidus for the first time in 1887, Davies Colley reported amongst his 5 cases 2 which occurred spontaneously. It is now generally recognized that in the large majority of cases the condition has a spontaneous onset without history of trauma, and that it starts during adolescence. There is, in the main, agreement as to the sequence of pathological events. In the earliest stage there is simple spasm of the short flexors of the great toe, producing limitation of dorsiflexion, and associated with a painful swollen metatarsophalangeal joint. The spasm disappears under anæsthesia during this phase, and movement can be obtained (Mau, 1928). Next contracture of the structures on the plantar aspect of the joint takes place, causing permanent limitation of movement; and finally there develops a true osteo-arthritis in the joint, with bony deformity of both articular surfaces.

The question why this sequence of events should arise in an isolated joint in a young subject is not clear. The initial spasm is obviously a protective phenomenon designed to prevent painful movement due to some inflammatory change, and various suggestions have been made to account for the change. The infective theory—synovitis secondary to focal sepsis—has been mooted and largely discarded from lack of evidence, and the theory of constantly recurring minor trauma due to some faulty mechanism in the functioning of the joint is most widely accepted. Just where the fault lies is not fully understood. Davies Colley originally suggested that the cause was an abnormally long great toe in an unyielding and insufficiently long boot. Nilsonne (1930) found that in the majority of his cases the first metatarsal was longer than the second. Monberg (1935) supports Nilsonne and also considers that an unduly long first phalanx may be a cause. High heels are blamed by Strombeck (1934). Almost all authors are agreed that the condition is associated with pes planus, and a popular conception of the aetiology is that the flattening of the longitudinal arch increases the length of the inner border of the foot, and so causes undue weight to be borne by the first metatarsal when the heel is raised (Cochrane 1927, Lloyd 1935, and others.)

Fifteen cases of spontaneous hallux rigidus, in 7 of which the condition was bilateral, have been studied in an attempt to elucidate the problem.

An analysis of age, occupation, and duration of symptoms is interesting. In every case except one—a child aged eleven in whom symptoms commenced six months after treatment for fractured patella—the occupation has been one which entails standing or walking for long periods. In 12 of the 15 cases the first sign of trouble has appeared at the age of fourteen or fifteen years, during the first year after leaving school and within a few months of starting work; while in another case the patient was employed as a cycle errand boy for four years after leaving school, and symptoms started three months after he changed this occupation for one which necessitated his standing all day. Of the remaining 2 cases, one was

the child of eleven, and the other a postman aged forty-four, who had had bilateral hallux rigidus and completely rigid flat-foot for many years, and could give no date for the onset. The inference to be drawn from this almost constant history is that hallux rigidus must be due to some dormant intrinsic defect in the foot, which tends to manifest itself as the foot becomes more rigid and unyielding and a comparatively sedentary life is exchanged for one which involves the strain of prolonged standing or walking.

These cases were examined in the light of existing theories. One patient had septic teeth, and one underwent an operation for appendicitis a year previous to the onset of symptoms, but apart from these two, though no bacteriological examinations were carried out, there was no evidence of focal sepsis in the remainder. Only two of the girls confessed to high heels, and males were equally affected. In 15 of the 22 feet the first toe was longer than the second; in the other 7 the toes were equal in length. The first metatarsal was longer than the second in 12, equal to the second in 5, and shorter in 3. One bilateral case was not X-rayed. Skinner (1932) found that in 323 recruits for the army, the great toe was longest in 175—well over half. Neither the long toe nor the long metatarsal occurs with sufficient regularity to afford a satisfactory explanation. The number of people who have these peculiarities without suffering ill effects must be very large, and some other factor must be sought.

An impression is given in *Table I* of the degree of flat-foot found. Only 4 of the 22 feet involved showed no evidence of it, and these were in the earliest cases. The remainder all had some signs of collapse of the longitudinal arch, slight in the younger patients, but becoming more marked as the age increased, until in *Cases* 7, 14, and 15 there was advanced deformity. Mau (1928) and Kingreen (1933) have both remarked that in early cases there is little or no associated flat-foot, whereas in later cases it is the rule, and frequently a patient seeking advice for painful flat-foot is found to have an established hallux rigidus. This observation is borne out by the above findings, and discounts the theory that hallux rigidus is secondary to pes planus, due to lengthening of the inner border of the foot. None of the earlier cases had sufficiently advanced planus deformity to give rise to any appreciable elongation, and by no means all cases of flat-foot develop hallux rigidus. While there is undoubtedly an association between the two conditions, the evidence strongly suggests either that the hallux rigidus comes first and the flat-foot follows, or that the two develop *pari passu*.

In view of this definite relationship it seems reasonable to envisage the possibility of there being some common factor which may be responsible for the development of both conditions, and in searching for the cause of hallux rigidus to scrutinize the known predisposing causes of pes planus.

Morton has demonstrated the importance of the first metatarsal segment in the maintenance of the longitudinal arch, and has described various developmental anomalies which, by rendering it incompetent in supporting the inner border of the foot, give rise to eventual collapse of the arch. These anomalies are: (1) An unduly short first metatarsal; (2) Posteriorly placed sesamoids; and (3) Hypermobility of the first metatarsal segment due to laxity of its plantar ligaments. He recognizes three criteria of this last condition—(*a*) clinically demonstrable hyperextension, (*b*) widening of the space between first and second cuneiforms, and (*c*) thickening of the second metatarsal shaft.

The cases under consideration were examined for these points. Only 3 of the 20 examined radiologically showed a short first metatarsal. The position of the sesamoids was found to be variable, the majority appearing to be placed rather more posteriorly than usual. But as this is a likely finding owing to the spasm of the short flexors, and in some cases flexion deformity of the toe, little importance is attached to it. The findings in the examination for the third condition are given in *Table I.*

Table I.—Examination for Hypermobility of First Metatarsal Segment in Cases of Hallux Rigidus.

Case	Sex	Age	Foot	Associated Pes Planus	Clinically Demonstrable Hyperextension	Wide Inter-cuneiform Space	Thickened 2nd M/T Shaft
1	F.	11	R	None	++	+	−
2	F.	14	R L	Tendency Tendency	+ ++	Indefinite Do.	− −
3	F.	14	L	None	+	+	+
4	F.	16	R	None	+ definite	−	−
5	F.	17	R	+ Callosity under 2nd m/t head	+	+	+
6	F.	21	L	+	+ slight	+	+
7	F.	22	R	++	−	−	+
8	M.	15	R L	+ Callosities under + 2nd m/t heads	++ ++	Indefinite Do.	+ −
9	M.	15	R L	Tendency. Callosities under 2nd m/t heads	++ ++	+ +	− −
10	M.	16	R	+	+ slight	+	−
11	M.	16	R L	+ +	+ +	Indefinite Do.	+ +
12	M.	17	R	None. Callosity under 2nd m/t head	−	+	+
13	M.	19	R L	+ ++	− −	+ +	− +
14	M.	24	R L	++ ++	− −	− −	+ +
15	M.	44	R L	+++ +++	− −	Not X-rayed	

It will be noted that hyperextension of the first metatarsal segment was clinically demonstrable in 14 of the 22 feet under consideration, that it was found without exception in all the younger patients, and that it tended to be especially evident in those cases with little or no associated pes planus. Of the cases in which it could not be demonstrated, all but one showed a well-developed planus deformity.

This finding is in accordance with expectation. In a young subject with an incompetent first segment, the second metatarsal supports the inner side of the foot and maintains the posture, but under the increased strain this second segment gradually gives way and allows the foot to fall inwards and a planus deformity to develop. When such collapse occurs, the slack in the first segment is taken up so that hyperextension can no longer be demonstrated clinically. During the process, however, the additional weight borne by the second segment causes gradual compensatory thickening of the compact bone of the shaft of the metatarsal, the extent depending on the duration of the condition and the degree to which the second segment withstands the stress. Such thickening is not to be expected in early cases, but its presence affords evidence of the existence at some period of relative incompetence of the first segment. Reference to the table shows that it was unusual in patients under sixteen years, but that it was almost always present above that age, and that it was the rule in those cases in which hyperextension was not clinically demonstrable. Widening of the intercuneiform space is difficult of assessment, and there is a temptation to condemn any gap shown radiologically between first and second cuneiforms as being abnormally wide. In X-raying the feet, the photographs were taken with the patient standing on the film with the feet parallel and the tube centred midway between the great toes, so as to obtain comparable pictures as far as possible, and it is only in those cases in which, after comparison with normal films, there has been no room for doubt, that the sign has been recorded as positive. It is seen to be inconstant, but in 10 of the feet yields corroborative evidence of the abnormality. One case, *Case* 12, was an exception in that there was neither clinically demonstrable hyperextension nor pes planus, but the other two criteria were both present, and, further, a callosity was noted beneath the second metatarsal head—an additional sign of an incompetent first segment.

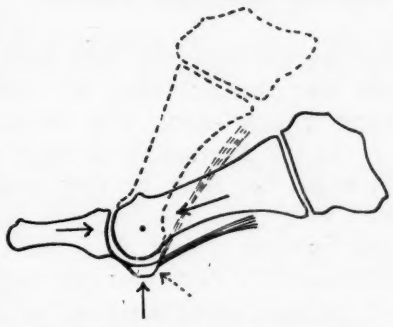

FIG. 353.—Diagram showing the rotation of the first metatarsal head about a fixed point, and the triangle of forces acting on it.

The foregoing data justify the assertion that in early cases of hallux rigidus hypermobility of the first metatarsal segment is a constant finding, while in later cases its previous existence can be shown. Can such a defect so alter the mechanics in the metatarsophalangeal joint as to occasion trauma?

The forefoot is composed of a set of five individual levers, each formed by a metatarsal bone and its associated tarsal bones, and having its fulcrum situated in the metatarsal head (Lambrinudi, 1932). In the case of the first segment, when the foot swings upwards as a step is taken, the metatarsal moves about a fixed axis situated in the centre of the head (*Fig.* 353). The short flexor incorporating the sesamoids passes directly below the head of the first metatarsal, and is angulated by it. During the upward swing the muscle gains in tone as it becomes stretched ready for the 'take-off', and at the same time the angulation increases. The effect of this action is the fixation of the first phalanx of the toe firmly to the ground, and also, owing to the angulation, the exertion of pressure on the metatarsal head in an upward and forward direction. This upward pressure is normally opposed by

the body-weight transmitted down through the metatarsal. A triangle of forces indicated by the arrows in *Fig.* 353 is thus constituted, which act on a point in the metatarsal head and hold it fixed.

The axis of weight-bearing is situated along the third metatarsal at the beginning of a step and gradually moves medially as the heel is raised, until just before the 'take-off' it lies midway between the first and second metatarsals (Elftman and Manter, 1934). If the first segment is incompetent, all the weight on the medial side of the axis is borne by the second metatarsal alone, provided it can withstand the strain, and no weight can be transmitted through the first segment until the axis has moved to the medial side of the second metatarsal. During the first stage of a step, therefore, the upward thrust of the short flexor is unopposed, with the result that instead of rotating normally, the head tends to ride forwards and upwards against the rim of the first phalanx, until the metatarsal assumes a sufficiently vertical position to drive it back again. The mechanism is shown in *Fig.* 354.

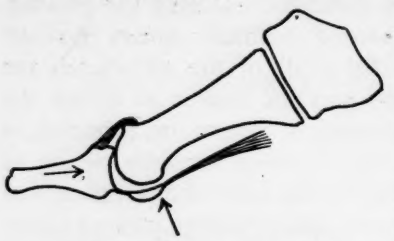

FIG. 354.—Diagram showing the elevation of the metatarsal head by the short flexor when hyperextension is possible.

In the diagram the range of abnormal movement is of course exaggerated, and in actual fact must be very small; but it is submitted that, constantly repeated with every step, this tendency on the part of the metatarsal head to push upwards and forwards against the upper rim of the fixed phalanx is sufficient to strain the attachment of the dorsal capsular ligament, and to traumatize the articular cartilage of the joint, particularly on the phalangeal side where the epiphysis is not consolidated. The reaction to this trauma is a protective spasm of the short flexor in an attempt to fix the joint, but this merely increases the upward thrust under the metatarsal head, and so aggravates the trauma.

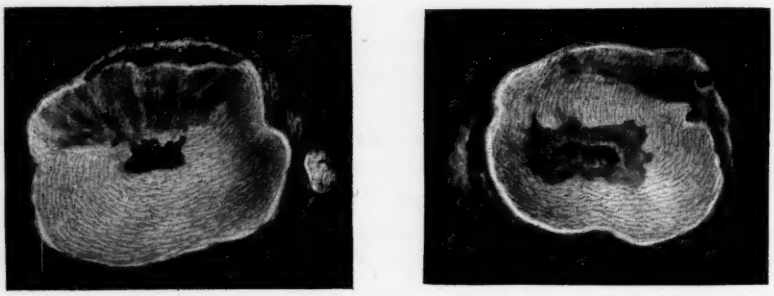

FIG. 355.—Drawing of two phalangeal articular surfaces showing the typical central and dorsal marginal erosions.

Finally, in support of this conception of the mechanism, the pathological appearances of the joint surfaces may be quoted; 9 cases of this series were subjected to operation, and in each case the joint was examined. In 1 case only was there any erosion of the articular cartilage of the metatarsal head. The phalangeal side, however, apart from minor variations, showed similar pathology in every case, and drawings of two of the articular surfaces demonstrate the typical appearances (*Fig.* 355). The dorsal and lateral margins showed osteophytic lipping

at the line of attachment of the capsular ligament. The articular cartilage presented two areas of erosion, one in the centre of the surface, which had probably developed after fixation of the joint, and the second along the periphery of the dorsal margin. This latter was usually the more marked of the two. Between the areas of erosion there was frequently seen a more or less wedge-shaped area which had lost its normal smoothness, and was roughened, injected, and often ridged in a vertical direction. In no case was the lower half of the articular surface affected. The constant situation of the erosions of the cartilage and of the osteophytic lipping is in keeping with the view of the aetiology propounded.

SUMMARY

In the examination of 22 instances of hallux rigidus occurring in 15 patients, it has been found that the condition precedes, or is coincident with, the early stages of pes planus. Practically every case affords definite evidence of an incompetent first metatarsal segment.

A mechanism by which this defect may be responsible for the development of both conditions is suggested, and the pathological changes found in the joint are cited in support of the suggestion.

My thanks are due to Mr. T. McW. Millar and Mr. D. S. Middleton, who were in charge of the Out-patient Department when these cases were seen—to the former for suggesting an interesting clinical problem, and to both for permission to investigate the cases and utilize the material. For the water-colour drawings in *Fig.* 355 I am indebted to Mr. R. W. Matthews.

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RADIUM IN TREATMENT OF CARCINOMA OF THE PROSTATE

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CARCINOMA of the prostate is not a rare lesion. It has been variously estimated (Young in Cabot's *Modern Urology*, 1936, vol. i, p. 829) to occur in 16–25 per cent of prostatic cases. That this figure is not an excessive one is borne out by the findings of Rich (1935) and Moore (1935). Rich (1935), amongst 2000 autopsies performed during three years, of which 292 were in men over 50, found carcinoma of the prostate present in 41, i.e., 14 per cent. Only a single section was made from each prostate. The carcinomata were in many cases only just visible, and some were microscopic in size. Of this material, 12 of 17 cases coming from the Genito-urinary Department, 1 out of 18 from the General Surgical Department, and 1 out of 16 from the Medical Department were diagnosed clinically. Moore (1935), using a section method of study, sections being made every 4 mm., found 63 cases of carcinoma of the prostate amongst 375 prostates of all ages, i.e., 16·7 per cent—in autopsies from hospitals in Vienna. B. Walthard (1938, quoted by Scholl et al.) found, from a study of serial sections, 30 cases of carcinoma in 100 prostates obtained from post-mortem material in patients over 40.

Caulk (1937) stated that 4 per cent of all cancer deaths are due to carcinoma of the prostate and 6 out of every 1000 deaths in the male are due to this cause.

PATHOLOGY

Moore (1935), in his series of cancer of the prostate, had 52 cases in which the lesion was small enough for the site of origin to be recognizable. He found 73·5 per cent of cases arising in the posterior lobe, i.e., the part of the prostate posterior and posterolateral to the fan-shaped ducts entering the sides of the urethra and which is half an inch below the bladder neck (Barringer, 1936). The area of carcinoma, in all but 2 cases which arose in an area of benign enlargement, was surrounded and infiltrated by glands typical of senile atrophy. The carcinoma arises from proliferation of epithelium which has already undergone atrophy. Although carcinoma of the prostate is associated in 50–60 per cent of cases with benign hypertrophy, the association is merely a fortuitous one. Moore found early invasion of the perineural lymphatics within the organ, but metastases and invasion outside the organ were late manifestations of the disease.

On the other hand, in clinical material evidence of local spread and infiltration as well as distant metastases is common. Barringer (1922) found evidence of spread towards the vesicles, bladder, and lateral pelvic wall, or distant metastases, in 142 of 145 cases. In 156 cases Barringer (1938) found 44 (28 per cent) with bony metastases. Amongst 396 cases of carcinoma of the prostate Hager and Hoffman (1937), in a statistical review, found metastases present in 107 cases at their first examination. Bumpus (1922)[1], in a series of 297 cases which were submitted to a routine X-ray examination of the chest, spine, and pelvis, found evidence of

bony metastases in 84 cases (28·28 per cent), and Burnam (1938) found metastases present in 59 cases out of a total of 158.

DIAGNOSIS

Carcinoma of the prostate may be broadly divided into the following groups :—

1. Pathological.—The patient complains of prostatic symptoms, a diagnosis of benign enlargement is made, and the pathologist diagnoses a carcinoma. Since it is very rare for a carcinoma to arise in an area of benign enlargement, simple removal of such an area—diagnosed by the pathologist as carcinoma—does not usually remove the whole of the growth.

2. Metastatic.—

a. Radiological.—The patient complains of persistent backache or sciatica, and a radiograph reveals the opaque metastases so typical of secondary prostatic deposits. Clinical examination of the prostate may fail to reveal any abnormality.

b. Clinical.—The patient complains of symptoms brought about by the presence of clinically recognizable metastases. In the search for the primary focus, the prostate may or may not be recognized as the cause.

3. Clinical.—The patient complains of prostatic symptoms which differ in no way from those found in benign enlargement. There may be additional symptoms due to the spread of the carcinomatous process. On rectal examination the prostate is found to be hard or irregular in consistency, and there may be evidence of local infiltration or spread. Since in the majority of cases the posterior lobe is involved, either alone or with other lobes, rectal examination will usually reveal the induration if the carcinoma is of any size. In a doubtful case aspiration biopsy is advocated amongst others by Barringer (1922, 1937) and Russel S. Ferguson (1930). Demonstrable material can be obtained in 60–80 per cent of aspirations, and is of value if submitted to a pathologist accustomed to dealing with such tissue.

RADIUM TREATMENT

Since its first reported use by Pasteau and Degrais (1913), radium has been applied in a variety of ways in the treatment of carcinoma of the prostate. Barringer (1922) used a steel needle 10–15 cm. long, No. 18 gauge, carrying 50–100 m.c. in the terminal 3 cm. This was inserted into each lateral lobe from the perineum and 300–400 m.c.-hr. were given to a mass 2 cm. in diameter. The treatment was repeated every two or three months till the prostate was sclerosed. In addition the vesicles were similarly irradiated, the needle having been inserted through the perineum or directly through the rectum. In later communications (1936) he advocates the use of interstitial irradiation of the prostate combined with deep X-ray therapy. A dosage of 1500–1800 mg.-hr. is given through the perineum every two months for six months if the posterior lobe is involved, or if the lateral and median lobes are affected 1·5-m.c. seeds are inserted suprapubically for each cubic centimetre of prostatic tissue.

Young (1922) gives a surface application of radium, applied by means of a special applicator through the rectum, the prostatic urethra, and the base of the bladder. A chart is kept on which the area of mucosa treated is marked, and no area is irradiated a second time until from two to three weeks have elapsed. Each application lasts an hour, and the whole course is spread over from six to eight weeks. This is combined with intraprostatic radium as suggested by Barringer.

Deming (1922), in a follow-up of Young's cases, concluded that 3000 mg.-hr. were necessary to produce local and symptomatic improvement, and suggested that 4000–5000 mg.-hr. should be given by surface application, together with 500–2000 mg.-hr. intraglandularly. The majority of the patients dealt with in the follow-up, however, received a much smaller dose.

At the Mayo clinic (Bumpus, 1922)[1] radium was at first given by rectal and urethral applicators, but later this was combined with interstitial irradiation. The average dose given was 1960 mg.-hr. Bumpus found that 400–600 mg.-hr. was a maximum safety dose for rectal mucosa, especially if there was also cross irradiation, and that 2500 mg.-hr. to the prostate was a maximum dose even in the largest gland, if considerable sloughing was to be avoided.

Burnam (1938) uses a radium bomb, believing that interstitial irradiation should be reserved for cases presenting the possibility of cure, i.e., in small growths with no distant metastases or marked local spread. He gives 100–300 g.-hr. through multiple portals at a distance of 7·5–10 cm. The treatment is spread over a period of from two weeks to three months.

Ferguson (1937) inserts 2-m.c. radon seeds suprapubically. He uses a perforated plate which is placed over the base of the bladder, a stop fitting into the urethra and keeping it in position. The perforations are 1 cm. apart and the seeds are inserted through them, the introducer being withdrawn 1 cm. at a time. A total dose of 15–40 m.c. is given—the average dose being 25 m.c. He uses interstitial radium only in tumours which are less than 4 cm. in diameter.

Nitch (1936) exposes the prostate from the perineum and inserts 14–18 mg. of radium partly (6 × 1 mg.) into the prostatic capsule and the rest (2 × 2 or 2 × 3 mg.) laterally, for ten days. In addition he opens the bladder suprapubically and gives a surface application of 50 mg. to the base of the bladder and an intra-urethral application of 5 mg. for twenty-four hours.

Caulk (1937) inserts 10–20 seeds of 1·5 m.c. and supplements this by X-ray therapy through four or five portals. He does not advocate exposure either perineally or suprapubically.

Eleven cases have been treated at the Liverpool Radium Institute. A suprapubic cystostomy and biopsy had been done elsewhere, prior to their admission.

The prostate was exposed by the perineal route, using a Young's long prostatic retractor, and needles were inserted into the body of the prostate and into lateral extensions in the region of the seminal vesicles. Needles were left in usually for seven days. The average dose was 4700 mg.-hr.

RESULTS

The results of treatment can be considered from the point of view of prolongation of life and of amelioration of symptoms. In order to assess the value of treatment, the natural history of the disease must be known. Unfortunately, carcinoma of the prostate varies considerably in the degree of malignancy. Guyon (Cabot's *Modern Urology*) divided cases into three groups :—

1. Those with a rapid course, in which the symptoms may have been present a very short time.

2. Those with a subacute course, the disease having been present after the tenth or twelfth month.

3. Those with a slow course, with a duration of two or three years and even as long as nine years.

Usually the younger the patient and the smaller the prostate, the more malignant it is, but there are many exceptions to this. The large glandular, nodular, adenocarcinoma is less malignant than the spheroidal-celled carcinoma (Judd, Bumpus, and Scholl, 1921). Bumpus (1922)[2] found that the average duration of life in 241 untreated cases was 32·04 months. Of these 229 were dead and had lived an average of 32·29 months. They lived a little over 10 months after the first examination.

Hager and Hoffmann (1937) in a series of 396 cases treated mainly by conservative surgery—there were 112 cystostomies, 76 resections, and 93 simple prostatectomies—found that 186 died in the first year, 31 patients lived three years or more, and 11 lived five years or more.

Table I.—COLLECTED RESULTS OF TREATMENT

AUTHOR	TREATMENT	TOTAL CASES	ALIVE 3 YEARS OR MORE	ALIVE 5 YEARS OR MORE
Radium :—				
Barringer (1936)	Interstitial	351[1]	47 (13·4 per cent) alive 29 (8·3 per cent) alive and well	23 (6·5 per cent) alive 20 (5·7 per cent) alive and well
Deming	Surface (R, U, B)	100	17 per cent	5 per cent
Bumpus (1922)	Surface (R, U) and interstitial	217[2]	8	
Burnam (1938)	Teleradium	125	17 (13·6 per cent)	8 (6·4 per cent)
Ferguson (1937)	Interstitial	43[3] (14 more than 3 years)	4 (28·6 per cent)	
Nitch (1936)	Interstitial and surface (U)	20		3 (15 per cent)
	Interstitial and surface (U, B)	7	5	2
Radium Institute	Interstitial	11 (1 alive)	2	0
Surgery :—				
Young (1937)	Radical prostatectomy	58	—	17 (53 per cent)
Judd et al. (1921)	Simple prostatectomy	146[4]	16	9
Hager and Hoffmann (1937)	Conservative surgery	396[5]	31	11

R, Rectum; U, Urethra; B, Bladder.

[1] 20 per cent too advanced for treatment.
[2] 29 living at time of writing, all less than 3 years.
[3] Of the 29 cases treated less than 3 years ago, 10 are dead, and 5 others are alive with evidence of carcinoma.
[4] 17 living at time of writing, all less than 3 years.
[5] 55 additional cases were alive at time of writing—all less than 3 years, and of these 36 less than a year.

The table (*Table I*) gives the number of patients who were alive 3 or 5 years respectively after treatment, and for comparison the results obtained by radical prostatectomy, simple prostatectomy, and conservative surgery are appended. Where the total number of cases includes a number still alive and treated less than 3 or 5 years before publication, the percentage is not added after the figure given.

The table does not demonstrate all the effect of radium in the prolongation of life. Bumpus (1922)[1], comparing the results of simple prostatectomy with radium, had better results with surgery, but he stressed the fact that the general condition of the former patients was better than the latter. In 29 patients treated by radium who were still living, the average duration of life following treatment was 28 months, compared with 27 months in cases treated by surgery. This is to be compared with the average duration of life of ten months after the first examination in the untreated cases. He gave a table which showed that although the number of cases alive at the end of each period of a year treated by surgery was double that given by radium, the cases treated by radium were twice as numerous as those untreated. He pointed out, however, that during part of the time radium treatment at the Mayo Clinic was still in an experimental stage.

Of the 20 cases reported by Nitch (1936) which died less than 5 years after treatment, 17 lived on an average 22 months.

Apart from the prolongation of life, radium has relieved symptoms. Deming (1922) found 75 per cent relieved of frequency and obstructive symptoms and 50 per cent relieved of pain. Burnam (1938) obtained relief of symptoms for a year or more in 65 of his 125 cases, including some with metastases. On the other hand, Barringer (1938) has not found retention of urine relieved by irradiation, and Bumpus (1922),[1] though finding that radium occasionally relieved symptoms, did not, from his experience, advocate its use solely for relief of such symptoms, if there were no hope of prolonging the patient's life—for example, in cases of bony metastases, when he found 73 per cent of 113 patients lived on an average seven months after the first examination.

The results obtained in the 11 cases treated at the Liverpool Radium Institute are given in *Table II.*

The numbers are too few to allow of any conclusions, but certain points are of interest. It will be noted that both wounds healed if the patient lived any length of time. The perineal wound in a fit patient was healed in three or four weeks. The symptoms, difficulty and pain on micturition, and frequency, improved—4 patients who had had retention could pass urine normally. On the other hand, in 5 cases the suprapubic wound had not healed in patients who had lived from one to eight months after treatment.

The first case is of interest in that, because of a persistent suprapubic fistula in a fit patient, an opportunity was had of examining the prostate at the time of the secondary operative closure four months later. It was found that with the dose of 2880 mg.-hr. (twelve 2-mg. needles, 0·8 mm. platinum filtration, for 120 hours), the prostate had completely disappeared. Unfortunately, as the size of the prostate is not known, its dose in r units cannot be approximately calculated. *Case* 9, with a larger dose of radium, showed necrosis and ulceration of the prostate at post-mortem eight months later. This factor of excessive destruction and necrosis, with consequent toxic absorption, was stressed by Bumpus (1922)[1], who pointed out that it might be too great a strain on kidneys already diseased. *Case* 11, with 4368 mg.-hr., showed no necrosis.

Case 3, who lived longest after treatment and who had had retention prior to his suprapubic cystostomy and biopsy, died of congestive cardiac failure, and at post-mortem there were metastases in the aortic glands as well as advanced pyelonephritis. A little thickening was present around his prostate. The fourth

Table II.—Results of 11 Cases at Liverpool Radium Institute

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Case No.	Age	Length of History	Symptoms	Pathology	Treatment	Duration of Life	Relief of Symptoms	Wounds Healed		Cause of Death
								Suprapubic	Perineal	
1	63	Mth. 2½	Retention, dysuria	Poorly differentiated adenocarcinoma	Mg.-hr. 2880	Mth. 19	Yes	Secondary operation closure	Yes	Uræmia. No post-mortem
2	65	1½	Retention	Carcinoma	4704	3½		No	Yes	Bronchitis, no secondaries
3	76	3	Dysuria, retention, frequency	Adenocarcinoma	3600	46½	Yes	Yes	Yes	Cardiac failure. Post-mortem: thickening round prostate; advanced pyelonephritis; secondaries in aortic glands
4	67	36	Dysuria, retention	Adenocarcinoma	5040	35	Yes	Yes	Yes	Readmitted with retention; uræmia. No post-mortem
5	53	12	Pain in back	Adenocarcinoma	4032	2		Yes	Yes	* Post-mortem: aortic glands and 7th dorsal vertebra involved in growth
6	71	24	Dysuria, frequency	Transitional carcinoma	9744	1½		No	No	Probably also renal infection
7	71	6	Dysuria, frequency, hæmaturia	Carcinoma	5208	1		No	No	Post-mortem: carcinoma spreading through pelvic cellular tissue; cystitis and pyelonephritis; no secondaries
8	65	3	Dysuria, frequency, retention	Anaplastic carcinoma	3840	2	No	No	No	Pain and wasting
9	68	12	Frequency, dysuria	Adenocarcinoma	4032	8		No	Yes	Uræmia. Post-mortem: secondaries in liver and pancreas; prostate ulcerated and necrotic; bilateral pyelonephritis
10	66	24	Dysuria, retention	Adenocarcinoma	3696	Alive 9	Yes; slight frequency	Yes	Yes	
11	76	5	Retention	Adenocarcinoma	4368	2		No	No	Post-mortem: small prostate with bilateral pyelonephritis; malignant glands along aorta.

* Radiograph of pelvis and lumbar spine four months before death showed no evidence of any metastases.

patient was re-admitted with acute retention just prior to his death. A soft rubber catheter was passed with ease, but he died thirteen days later. Unfortunately a post-mortem examination was not permitted.

DISCUSSION

Opinion is divided as to the value of radium in the treatment of carcinoma of the prostate. Many surgeons believe that it is impossible to cure carcinoma of the prostate, that attempts to do so may bring complications in their train which make the patient's lot worse, and that since the evolution of the disease is a slow one, treatment should be limited to conservative surgery, either endo-urethral resection or a suprapubic cystostomy. This defeatist attitude is an unfortunate one. Endo-urethral resection is not of use in growths which begin centrally and invade the prostatic urethra, and is contra-indicated in rapidly growing cancers, where relief, if secured, is of short duration (Nitch, 1936). Thus the end of many patients would be rendered miserable by a suprapubic cystostomy.

The pathological work of Rich (1935), Moore (1935), and Walthard (1938) tends to show that cancer of the prostate is comparatively slow in its progress, but a review of clinical material shows that the duration of life from the commencement of symptoms is not so prolonged. In Hager and Hoffman's (1937) series of 396 untreated cases, 186 deaths occurred within 1 year. Barringer (1936) found that of 322 non-controlled cases of carcinoma of the prostate treated by radium, 243 died within 2 years. Bumpus (1922)[2] found that out of 241 untreated patients, the average duration of life was about 32 months, and that they lived an average of 10 months after the first examination. Treatment, therefore, should be attempted; but if the possibility of cure is remote, care must be taken to avoid distressing complications in carrying out any form of therapy.

Radical surgery has, in the hands of Young and one or two others, had brilliant results. Young (1937), in a follow-up of his cases, reported only 58 radical prostatectomies for cancer—the first case being in 1905. It would appear that the operation is indicated but rarely, and cannot be considered an important factor in the treatment of the disease at present. The majority of urologists have been disappointed with their 5-year ' cure ' rates, and have been impressed rather with the relative frequency of stricture and incontinence following upon the operation.

The results of radium cannot be said to be brilliant, but radium usually prolongs life in the average case, and the number of 3-year and 5-year ' cures ' is greater than in the untreated cases. Unfortunately, complications have occurred, but these mainly in the past, and especially when heavy doses have been applied to the rectal mucosa. Deming (1922), in a follow-up of Young's cases, had 4 cases of rectal ulceration and 1 of fistula, and Ferguson (1937), in his first 14 cases done over three years, had 2 urethro-rectal fistulæ. The immediate mortality is low.

CONCLUSIONS

Radium has a definite place in the treatment of carcinoma of the prostate. To be of maximum benefit irradiation should be uniform, and since massive local destruction is to be avoided, multiple foci of low intensity should be used. The perineal exposure of the prostate allows of a uniform distribution of needles, without concentrating the dose at any mucosal site. Extension of the growth in the

neighbourhood of the vesiculæ seminales can also be dealt with. In cases with marked sepsis or kidney inefficiency, these must be dealt with by preliminary drainage, either by indwelling catheter or by suprapubic cystostomy. There were no vesico-rectal fistulæ and no immediate mortality from the perineal operation in this small series, though a number of the patients were poor subjects.

Radium is not of universal applicability. The patient with distant metastases and with pain referred to the lower limbs, usually due to glandular metastases in the pelvis, is better not treated with radium. About a third of patients have demonstrable metastases when first seen. If the general condition of the patient is poor or the kidneys are inefficient, radium should not be used unless and until improvement takes place. When there is marked obstruction conservative surgery should usually be carried out in addition to radium therapy. Patients treated with radium should be followed up carefully, as in the event of fibrosis occurring dilatation or endo-urethral resection may be necessary.

For treatment to be of value in cancer of the prostate, the condition must be diagnosed earlier. It seems that this can only be accomplished by a routine six-monthly rectal examination in people over 50, which may reveal areas of induration, the pathology of which can be confirmed by aspiration biopsy. In these early cases the results of treatment by radium will almost certainly be better than those hitherto published.

SUMMARY

1. Radium has a place in the treatment of carcinoma of the prostate, but is not universally applicable.

2. Only a proportion of cases derive benefit from treatment, and in those in whom life is not prolonged, the condition is at any rate not aggravated.

3. The open perineal route allows of adequate access and uniform irradiation.

I am very much indebted to Mr. F. Strong Heaney for permission to publish these cases, which were admitted under his care. I should also like to thank Dr. H. H. MacWilliam and Mr. A. Kirk Wilson for the post-mortem reports.

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PLETHYSMOGRAPHY OF THE SKIN IN THE INVESTIGATION OF PERIPHERAL VASCULAR DISEASES

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INTRODUCTION

PLETHYSMOGRAPHY has been used in man and animal by numerous investigators to elucidate the reaction of the vascular bed of different organs to certain stimuli such as cold and heat, injections of drugs, or nerve stimulation. A good deal of our knowledge concerning the regulation of the peripheral blood circulation is based on experiments carried out by this method.

Until recently plethysmography as applied to man was only of more or less scientific interest and was mainly used in the investigation of physiological and psychological reactions (Mosso,[34] Bowditch and Warren,[9] Piotrowski,[39] Francois-Franck,[15] Swammerdam,[45] Lehmann,[27] Berger,[4] Weber[47]) rather than for clinical studies. The reason seemed to be a technical one. Investigations with the older types of plethysmographs demanded considerable technical skill in order to obtain reliable results, since the types of apparatus used were not sensitive enough, and the whole limb—arm or leg—had to be enclosed to obtain changes sufficiently large for satisfactory recording. Many errors were entailed and the method was therefore much neglected. However, the results obtained by some of these authors,[4, 27, 45] with this type of apparatus are still valid (Berger[5]).

Such sources of error in the limb plethysmography have been recognized as movements of the whole limb or contractions of the enclosed muscles, which are difficult to avoid since they may be subconscious. How difficult it was to interpret registered volume changes is best illustrated by the fact that a considerable number of authors (Lehmann,[27] Berger,[4] Weber,[47] Uhlenbruck,[46] Mosso,[34] Fick,[14] Buisson,[8] Francois-Franck,[15] Piegu,[37] Bruns and Schmidt[10]) described volume changes simultaneously with the respiration as vasomotor reactions, while others definitely maintain that the waves are mechanically produced by movements of the arm simultaneously with movements of the chest (Hewlett and van Zwaluwenburg[24] and Dessecker and Steinhausen[12]), or by movements of groups of muscles which are enclosed in the plethysmograph contracting simultaneously with the respiratory movements (Roemer and Hoernicke[41]).

Since, beside the skin, considerable masses of muscles were enclosed in the limb plethysmograph, the changes registered by the plethysmograph were consequently a mixture of the reaction both of the vessels of the muscles and those of the skin.* However, skin and muscle vessels may either react in the same or in the opposite way to the same stimulus (Rein,[40] Pieren,[38] Donegan,[13] Grant and Pearson[20]),

* This holds good also for those types of plethysmograph in which only the hand, foot, or a part of the forearm were enclosed. (Hewlett and van Zwaluwenburg,[24] Freeman,[16] Stead and Kunkel,[44] Lewis.[28]

thereby further complicating the interpretation of the volume changes occurring in the limb plethysmograph, which is thus liable to be ambiguous (Hess[23]).

For clinical purposes, however, where methods generally used in animals to determine the part played in the reaction by one or the other group of vessels can seldom be applied, it is desirable to have a method by which a single tissue—the skin—can be investigated without incurring the above-described difficulties of limb plethysmography.

It is only recently that plethysmographs have been constructed which can meet these demands. By the application of optical and photo-electric principles the method became sensitive enough to make visible the registrable changes in smaller portions of the circulation—the fingers and toes—and consequently allowed quantitative as well as qualitative comparison from one experiment to another. Thus it became possible to measure changes in the blood content of the human skin only, opening for investigation by this method the vast field of circulatory diseases in general and that of the peripheral vascular diseases in particular.

Despite the fact that the plethysmographic methods proved to be of important clinical value, they are not frequently used in the clinical laboratory, partly because they are not sufficiently well known, and partly because they are considered to be too complicated for such use. We therefore propose to discuss here the principles used in different plethysmographic methods and to give the construction of the apparatus. An interpretation of the nature of the volume changes seen in the records is given in order to enable the clinician to apply the method.

METHODS AND THEIR UNDERLYING PRINCIPLES

The different methods which measure changes in the blood-flow of the skin can be divided into the following groups according to the underlying principles: (1) Methods of the transmission type; (2) Methods which make use of photo-electric effects; (3) Di-electrographic methods.

1. PLETHYSMOGRAPHS OF THE TRANSMISSION TYPE

Principle.—The principle of this type is too well known to need much discussion. Changes in the volume of the skin during rest or during the short time of the experiment are assumed to depend solely on changes in the blood content. To transmit the changes to the recording system the skin has to be enclosed in a suitable container (plethysmograph). Thus the regions which can be investigated by this method are limited to the fingers, toes, and ears. The changes occurring in these organs can be attributed to a single tissue, since the bones, cartilages, and tendons have a blood-supply serving for nutrition only, and can be taken as constant for the duration of the experiment.

The Choice of Plethysmograph.—The finger plethysmographs used in this method are all constructed on the same principle. We will describe therefore only those types which we developed[17, 18] and found most suitable (*Figs.* 356, 357).* Plethysmographs of glass have the advantage that changes of the skin colour can be observed during the course of an experiment and congestion can be controlled when the plethysmograph is fixed. For the fingers a set of glass tubes 8 cm. long,

* Various types of finger plethysmographs have already been described by Sewall and Sanford,[43] Lombard and Pillsbury,[30] Siebeck,[43] and Lewin.[28]

and with various diameters between 15 and 30 mm. to fit every size of finger, served as plethysmographs. These tubes were drawn out at one end into a tube of 4 mm. diameter and 6 cm. in length (*Fig.* 357). For the toes, tubes of 6 cm. length

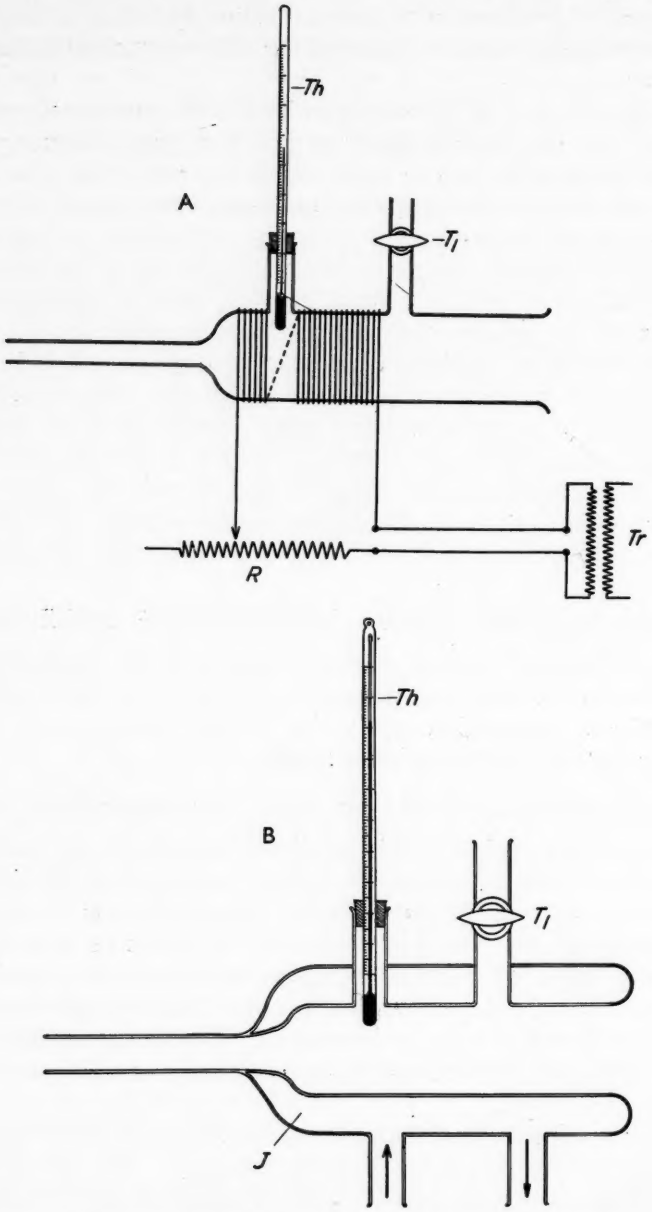


FIG. 356.—Finger plethysmographs. A, Fitted with a heating coil fed from a transformer (*Tr*) over a variable resistance (*R*) to keep the temperature constant above room- or skin-temperature. B, Fitted with a jacket (*J*) to keep the temperature constant below room-temperature. (*Th*) Thermometer; (*Tl*) Tap.

and a diameter varying between 1·5 cm. and 3·0 cm., but otherwise of the same shape, were used. The plethysmograph (*Pl*) is fitted with a glass tap (T_l) projecting

vertically from the side, to allow the air to escape when the finger is inserted or the plethysmograph filled with water. A thermometer (*Th*) is inserted into the apparatus. After bringing the finger into the plethysmograph the temperature very soon reaches equilibrium, especially when the plethysmograph is covered with cotton-wool. For tests in which the temperature should be kept constant at a level above that of the room or even above that of the skin, a heating element is coiled round the plethysmograph, fed from a 6-volt transformer (*Tr*) with an output of about 25 watts (*Fig.* 356, A). A resistance (*R*) serves to regulate the temperature; a self-regulating heating device can easily be mounted, but has been found superfluous since the temperature readily remains constant at the adjusted level. For certain experiments, however, it should be possible to lower the local temperature. Plethysmographs of the form shown in *Fig.* 356, B have been developed for this purpose. Water of known temperature from a reservoir runs through the jacket (*J*), thus cooling the plethysmograph, containing the finger, to the required temperature.

The choice of a plethysmograph of the correct size is of great importance. It should be big enough to avoid any possible venous congestion, and allowance should be made for possible expansion of the organ occurring experimentally during the tests. This, however, can easily be controlled. The choice of the correct plethysmograph should on no account be left to the patient, who will always choose one that is too tight.

For sealing, many investigators[24, 25, 27, 28] use a perforated rubber diaphragm, and others rubber and putty.[38] This, however, we do not consider to be satisfactory, and we believe that venous congestion will occur very easily, especially if in certain tests the volume of the finger increases. We therefore recommend a grease with a high melting-point, as is used for motor cars. Thus practically no pressure will be placed upon the skin whatever the state of the blood content of the finger may be.

Transmission and Recording of the Volume Pulses.—Different ways have been developed to record the changes in volume occurring in the plethysmograph. Some are needlessly complex and the details of construction are often not available. In principle the recording system should have the following qualities: (1) It should be sensitive enough to register the volume changes occurring with each heart-beat instantaneously. (2) It should be of such a size that every detail can easily be seen, measured, and compared in different experiments. (3) No distortions of the volume pulses should occur, since the shape will be found to be significant for different pathological conditions. (4) The registration system should not interfere with the blood-flow in the organ measured and no pressure should be applied to the surface of the organ. Especially no change in pressure should occur with changes in volume. (5) The inertia of the recording system should be small enough to be negligible. (6) The system should always be calibrated and the calibration should give a straight line.

These conditions are definitely not fulfilled by the older systems where the plethysmograph is connected to a Marey tambour or a piston recorder and the tracings are made on smoked paper. The optical methods are better. They were first applied by Baldes and Corbeille.[3] These authors, however, transmitted the volume changes by air to a water manometer. They photographed the changes in pressure and converted them into changes of volume by the use of the following equation:—

1. The volume V_0 (in c.c.) of the organ placed in the plethysmograph is given by:

$$V_0 = \frac{p}{h} (\Delta V - \Delta V_1) \text{ (according to Boyle's law)}$$

wherein p = atmospheric pressure (in cm. water); h = increase in pressure (in cm. water) in the water manometer brought about by a decrease in volume of the closed system of ΔV_1; ΔV_1 = the decrease in volume of the closed system which increases the pressure by h; ΔV = decrease in volume of the empty plethysmograph which increases the pressure by h.

2. The increase in volume of the organ (ΔV_x) which increases the pressure by h_x is given by the following equation:

$$\Delta V_x = \frac{h_x}{p} (\Delta V_1)$$

wherein, h_x and ΔV_1 are as defined above.

However ingenious this method may be, it is not suitable for clinical investigations since the volume changes are not directly registered and have first to be calculated. Secondly, changes in pressure within the system occur which may interfere with the blood-flow in the capillaries and veins. This argument holds good also for the apparatus recently described by Bolton, Carmichael, and Stürup.[6] These authors simply replaced the water manometer by a membrane manometer.

These limitations have been overcome, and a method registering only volume changes, which meets all the above-mentioned principal points, has been developed by the author.[17, 18] The principle is that the plethysmograph is connected with

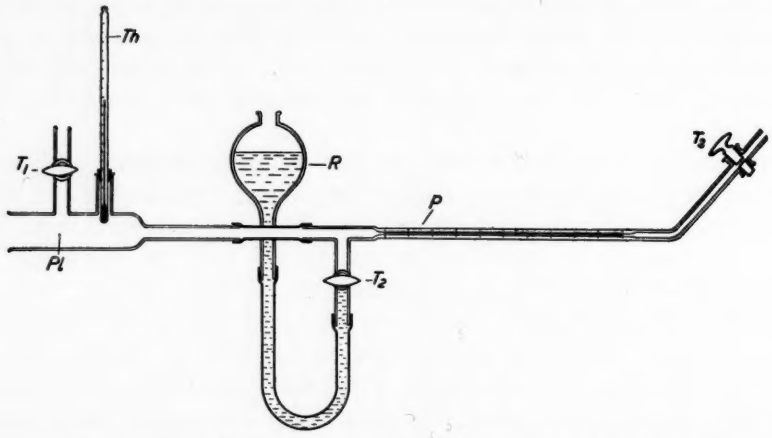


FIG. 357.—Plethysmograph (*Pl*) connected to the pipette (*P*) for the registration of the volume. A reservoir (*R*) is connected to the pipette to replace the air in the pipette and the plethysmograph by water.

a calibrated pipette (*Fig.* 357). The volume changes occurring in the plethysmograph are transmitted by water to the pipette, magnified, and recorded by optical means. Photographing the volume changes in the pipette is possible without staining the liquid by taking advantage of the following optical effects (*Fig.* 358): (1) The empty pipette (*P*) behaves to the light like two parallel glass plates; while (2) The part in the pipette filled with water (*W*) reacts like a cylindrical lens. (3) The water surface in the pipette forms a meniscus which refracts the beams, thus producing a shadow giving a white band on the paper. (4) The calibration of the pipette appears on the paper as shadows simultaneously producing white lines.

The system is therefore always and for each magnification automatically calibrated in 0·01 c.c., and volume changes down to 0·001 c.c. can easily be measured.

The plethysmograph (*Pl*, *Fig.* 357) is connected by 8 to 10 cm. pressure-tubing (3-mm. bore) to a 1-c.c. pipette (*P*) calibrated in 0·01 c.c. A T-piece fitted with a tap (T_2) is fused on to the pipette, for which purpose the calibrated end of the latter has been cut off. The other uncalibrated end is bent upwards at an

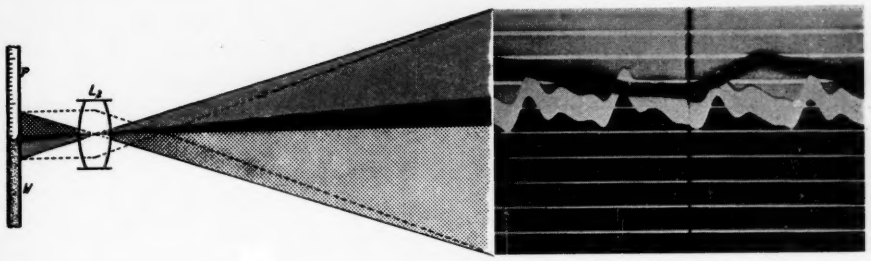


FIG. 358.—The optical principle by which it is possible to register the movement of the water column in the pipette. For description *see* text.

angle of 45°, and fitted with a tap (T_3). The pipette is mounted horizontally on a stand of the optical bench (*Fig.* 359, *P*) and illuminated by a lamp (*L*),* and by an ordinary diascope condenser (L_1) (10 cm. in diameter, 12 cm. focus). The pipette is photographed on the paper of a camera (*K*)† by a Zeiss Microtar objective (L_2) (or a corresponding substitute, as they are fitted as low-power objectives in microscopes). The usual magnification applied, which can easily be changed in a few seconds, even during the tests, is between 2 and 6 times. Ordinary rubber tubing

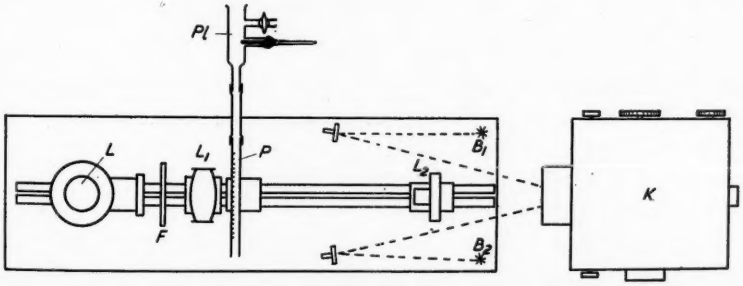


FIG. 359.—The pipette (*P*) is mounted horizontally on the optical bench, illuminated by the lamp *L*, and enlarged by the optical system L_1 and L_2, to be photographed by the camera *K*. B_1 and B_2, Arrangements for the simultaneous registration of other functions such as respiration, venous pressure, or the pressure in a cuff to apply a venous congestion test.

connects the pipette via the tap T_2 (*Fig.* 357) to a 100–200-c.c. reservoir, allowing the air in the pipette and the plethysmograph to be replaced by water.

For the test the individual may either sit comfortably in a chair if the fingers are to be tested, or lie or sit in half-recumbent position on a bed in the case of the toes being investigated. Supports are fixed so that the fingers or toes are at the level of the horizontally mounted pipette. The finger is inserted into the plethysmograph,

* 6-volt, 18-watt headlight bulb, fed from a second tapping of the transformer already used for heating the plethysmograph.

† A good and sturdy camera is made by Hellige, Freiburg i. B.

and the plethysmograph sealed and filled with water at body temperature by lifting the reservoir (*R*) (*Fig.* 357)* somewhat above the level of the pipette and by opening the taps T_1 and T_2 while tap T_3 is closed. The air in the plethysmograph being replaced by water, tap T_1 is closed and tap T_3 opened to fill the pipette, until the surface meniscus of the water column in the pipette enters into the centre of the field of light. Tap T_2 is then closed. The finger is now connected to the pipette only, and the water in the pipette can easily be seen to pulsate in a normal person. The volume changes can now be registered. Since the pipette is horizontally mounted on the optical bench at the level of the tested finger, no pressure is applied to the finger during the course of the experiment and no change in pressure in the plethysmograph occurs simultaneously with changes in volume. On the other hand the inertia of the water in the pipette is negligible and can be ignored. *Fig.* 360 is a typical tracing of a normal subject.

If the meniscus moves out of the optical field *adjustment* can easily be obtained within a few seconds by lowering or elevating the reservoir as necessary and opening

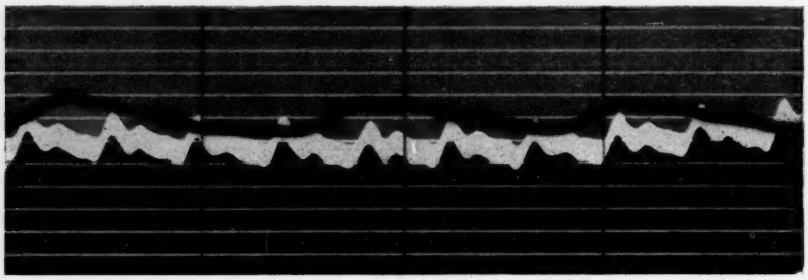


FIG. 360.—Plethysmogram of a normal subject. Second right finger. Room temperature, 23° C. Skin temperature, 31·5° C. Ordinates, 2 sec.; Horizontal lines, 0·01 c.c. (Mr. E. J. H.) R, Respiration (inspiration upwards).

tap T_2 until the meniscus reaches the desired point. For experiments of long duration it is further often a good practical measure to smear the finger with vaseline in order to prevent the skin from taking up water.

Sources of Error.—Sources of error arise from movements of the finger within the plethysmograph or of the whole hand together with the plethysmograph. These movements, however, can easily be controlled if the arm or leg on which the plethysmograph is fixed is resting comfortably. They are further easily recognized in the tracing. The patient is always conscious of movements which disturb the tracing.

Other errors may be introduced by changes in the temperature of the enclosed limb in the plethysmograph. If a rise in skin temperature by dilatation of the vessels occurs, the finger will heat both the plethysmograph and the water. Expansion of the water inside the plethysmograph will simulate a much larger increase in the finger volume, while the expansion of the plethysmograph tends to diminish an increase occurring in finger volume. Since the expansion coefficient of water is much greater than that of the glass, the volume of the water will increase to a much greater extent.

* This is best fixed on a stand with rack and pinion, but can also easily be fixed with a piece of string and a counter-weight.

If E_w is the expansion of the water and E_{gl} the expansion of the glass, E, the apparent expansion of the water, as observed, will be:

$$E = E_w - E_{gl}$$

E_w, for the water volume V_w and for the temperature change t, is given by:

$E_w = c_w \cdot V_w \cdot t$ (wherein c_w = the cubical expansion coefficient).

E_{gl}, under the same conditions for the volume V_{gl} of the plethysmograph and the temperature change t, amounts to:

$E_{gl} = c_{gl} \cdot V_{gl} \cdot t$ (c_{gl} = cubical expansion coefficient for glass)

Therefore:

$$E = (c_w \cdot V_w - c_{gl} \cdot V_{gl})\ t$$

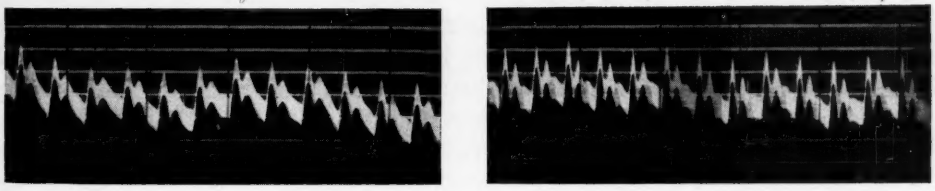
The volume of a plethysmograph of 8 cm. in length and 2 cm. in diameter is approximately 25 c.c., and an average second finger has 15–18 c.c. volume; V_w therefore is maximally 10 c.c. If we suppose the temperature changes from 20° to 30° C, the apparent expansion E will be given by:

$$E = (0{\cdot}00025 \cdot 10 - 0{\cdot}000025 \cdot 25) \cdot 10 = 0{\cdot}018$$

(c_{gl} being $2{\cdot}5 \times 10^{-5}$ and c_w being 25×10^{-5}.)

Since the volume increase of the finger due to dilatation in a normal person amounts on an average to 1·0 c.c., the error introduced by heating of the water and plethysmograph is roughly 2 per cent only.

Other Methods of Transmission.—Methods devised by Johnson[25] and by Matthes[31] also make use of a capillary tube. Beside other differences in the method employed by Johnson and ourselves, Johnson uses air to transmit the volume changes to a drop of coloured alcohol in the pipette. This has the advantage that the patient's hand or foot need not be at the level of the pipette. However, the air reacts like a cushion, thus leading to distortion of the volume pulses best illustrated



A B

FIG. 361.—The volume pulse of a normal subject. Second right finger. A, The correct shape of the pulse obtained with water transmission; B, Distortions in the shape of the volume pulse produced by air transmission. Ordinates, 2 sec. Horizontal lines, 0.01 c.c.

by *Fig.* 361. Since the shape of the volume pulse has been found to be of great value in the interpretation of pathological changes, one should not forgo the advantage of its correct registration.

The method of Matthes,[31] on the other hand, is needlessly complex, but has the advantage that the finger plethysmograph can be used in connexion with an already available electrocardiograph. The water in the capillary tube is darkly coloured, illuminated, and moves in front of a photo-electric cell.* The changes in volume give rise to changes in the potential of the cell which can be recorded by a string galvanometer. Sources of error, however, appear in the quality of the photo-electric cell, in which points of the surface lying beside each other vary in their

* A similar arrangement has been used in other connexions by the author.[19]

sensitivity to light up to 20 per cent.[31] In order to avoid this error it is advisable to use the capillary tube as a shutter to the source of light projected on the photo cell as a point, thus changing the intensity of the light, but not the area striking the cell. *Fig.* 362 is a tracing obtained by this method.

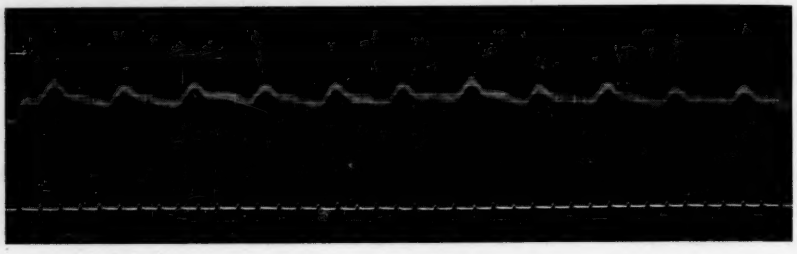


FIG. 362.—Registration of the movements of the water column in the pipette by means of a photo-electric cell (rectifier type) and a string galvanometer. Calibration of the sensitivity, 0·10 millivolt, on the left-hand side of the tracing. Same subject (Mr. E. J. H.) as *Fig.* 360. Second right finger. Room temperature, 23° C. Time marks, 1·0 and 0·2 sec.

2. PHOTO-ELECTRIC PLETHYSMOGRAPHIC METHODS

Principle.—These methods are based on the fact that the skin and subcutaneous tissues are translucent and that the amount of light passing through them can be measured with a photo-electric cell of either the emission or the rectifier type. The changes of its potential are proportional to the amount of light which strikes the cell and can be recorded either directly by means of a highly sensitive galvanometer of a very short period in the case of the rectifier type or after amplification if the emission type is used. These and the following methods definitely offer advantages as compared with plethysmographic methods of the transmission type: firstly, they abolish the use of a container; and secondly, the regions to which they can be applied are theoretically not limited. On the other hand, as will be discussed later, limitations are set to these methods where the transmission type described above still furnishes important results.

Two different types of photo-electric plethysmography have been developed. One group of authors measures the light actually passing through the tissues such as fingers, toes, or ears, by a red-sensitive photo-electric cell of the rectifier type (Matthes and Hauss,[32] and apparently also used by Hertzman[21]),* while Hertzman[22] measures the light that scatters in the skin only. Theoretically the latter method is capable of general application. In practice, however, its usefulness is very much limited by movements, and it is not possible to apply this type, for instance, in the measurement of the blood-flow in the skin of the trunk (Hertzman[22]).

Since the changes of the potential of the cell depend on: (1) The amount of light passing through the tissue, or, in other words, on the absorption of light by the tissue; (2) The amount of blood present in the tissues; and (3) The ratio of oxyhæmoglobin to reduced hæmoglobin (the colour of the blood), the tracing will record changes in blood-volume only provided the colour of the blood does not change. The absorption of the tissue can be taken as being constant, and normally the oxygen content of the blood will be practically constant if the respiration is

* This arrangement has been first used by Bonsmann[7] for blood-pressure measurements in rats.

quiet (Matthes and Malikiosis[33]). However, the application of this type of plethysmography is limited to those tests which do not entail changes in the utilization of the blood-oxygen.

Other difficulties are concerned with the calibration of the photo-electric plethysmograph, since the methods are only semi-quantitative. The comparison of the height of the recorded changes from one patient to another is not possible. Matthes used, therefore, the quotient obtained by dividing the total amount of light absorbed by the tissues into the amount of absorption brought about by the fluctuations. Hertzman obtained semi-quantitation by comparing the size of the waves with the changes of deflection obtained after inserting a glass filter.

Method.—Since I cannot offer experience of the method described by Hertzman, I can only draw attention to his excellent papers[21, 22] in which the method is described in full detail. The arrangement developed by us to measure the blood-flow through the skin by photo-electric methods is given in *Fig.* 363.

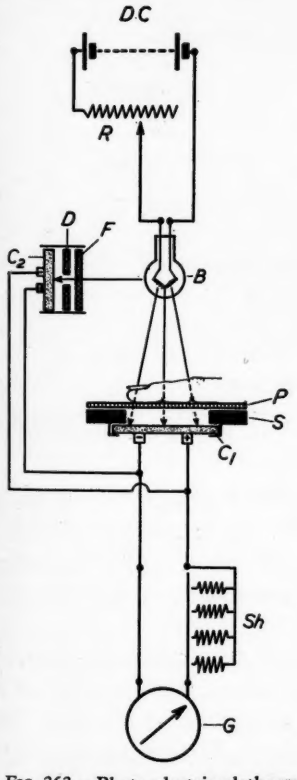


FIG. 363.—Photo-electric plethysmograph *B*, Bulb; C_1 and C_2, Photo-electric cells (rectifier type); *D*, Diaphragm; *D.C.*, Battery; *F*, Filter; *G*, Galvanometer; *P*, Glass plate; *R*, Variable resistance; *S*, Stage; *Sh*, Shunt-box of d'Arsonval type.

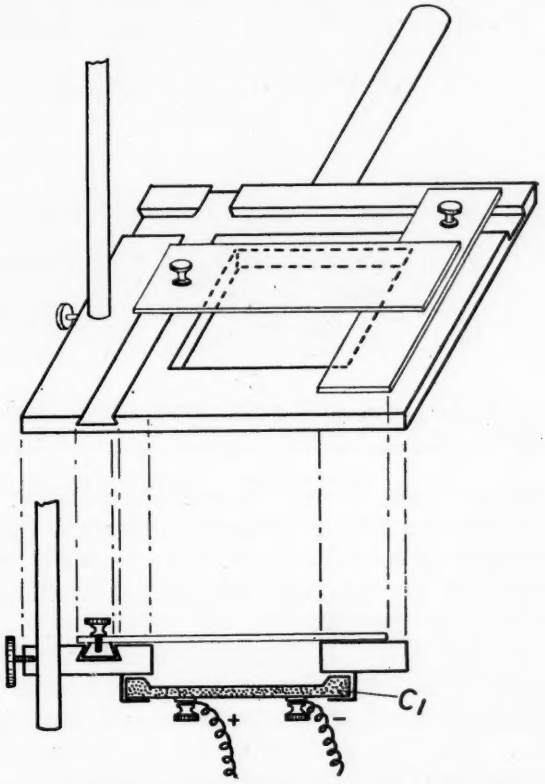


FIG. 364.—Stage with sliding screens and photo-electric cell as used in *Fig.* 363.

The light of a strong bulb (8-volt, 50-candle-power motor-car headlight bulb fed from a 10-volt battery) passes through one or many fingers of a subject which are resting comfortably on the glass plate *P*, fixed on top of the opening of the stage *S*, which can be adjusted by two sliding screens, according to the number and size of the fingers used (*Fig.* 364). The light passing through the tissue strikes the

photo-electric cell C_1 (rectifier type), fixed underneath the opening of the stage. The changes in the potential are transmitted over a shunt-box (*Sh*) to a highly sensitive Kipp galvanometer with a short period (0·01 sec.). The movements of the galvanometer are registered on the paper of the camera.

The amount of light passing through the tissues generates a constant output of current (basic current) in the cell. This is large, compared with current due to the changes in absorption, and the fluctuations brought about by changes in the finger volume, and deflects the mirror of the galvanometer very much. Since the deflections of the galvanometer are proportional only to the current within a small angle of the deflection from zero, a straight calibration line is not obtained and distortions occur. These complications have been overcome by coupling a second photo-electric cell C_2 (*Fig.* 363) illuminated by the same source of light within the circuit so that the current generated opposes that of cell C_1. By means of the iris

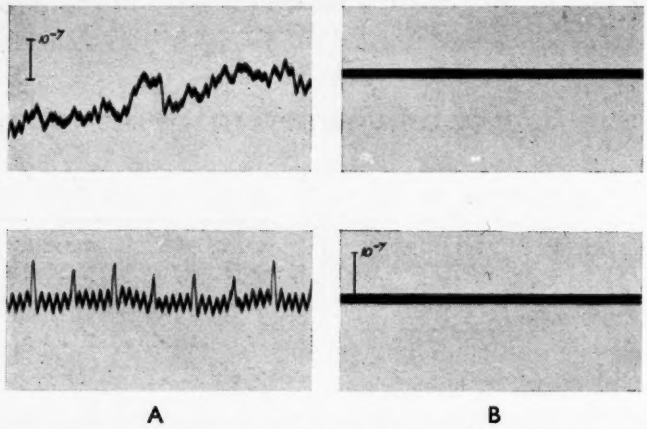
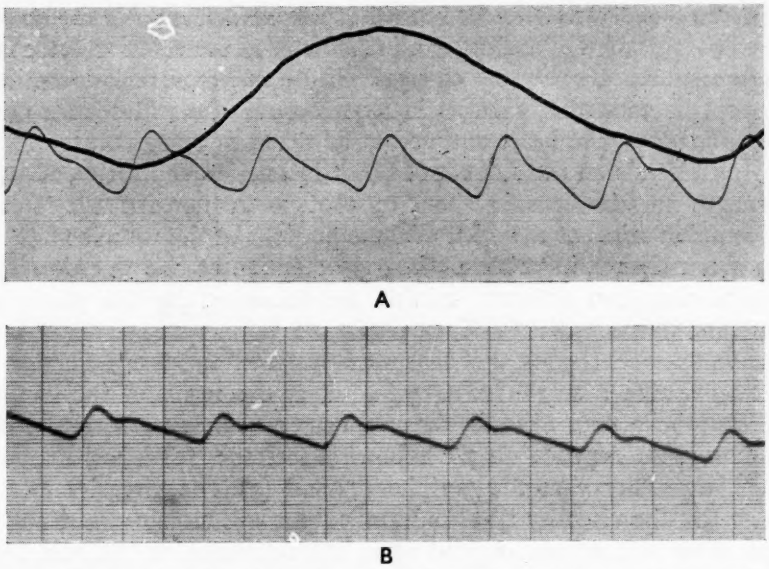


FIG. 365.—Complete elimination of changes in the intensity of the source of light by the arrangement given in *Fig.* 363. A, Current generated by one cell only (d.c. above, and a.c. below); B, The currents of the two cells oppose and nullify each other and a straight line is obtained.

diaphragm *D* and filters *F*, we are able to adjust the amount of light falling on cell C_2 so that the current generated will equal that of the basic current of cell C_1. Flowing in opposite directions the currents will nullify each other. The fluctuations brought out by changes in the volume only will now be recorded and the calibration will be a straight line.

It is obvious that the source of light should be absolutely constant, otherwise changes in the deflection of the galvanometer brought about by changes in the intensity of the light will be taken as due to changes in the blood-volume of the tissue. The bulb is therefore fed by direct current from a battery, preferably of high amperage, and all connexions soldered. Any remaining change in the intensity of the light can be completely eliminated (*Fig.* 365) by using the second cell (C_2) in the following manner (*Fig.* 363): We regulate first the opening of the stage required for registration, and by means of the diaphragm *D* we adjust the current of cell C_2 until *no* current-flow is indicated by the galvanometer, *G*. After placing the finger or toe upon the stage, which acts like a filter, part of the light formerly reaching cell C_1 will be absorbed and more current will now be generated by cell C_2 than by C_1. For this reason the light reaching cell C_2 is cut down by inserting filters (*F*) until the beam of the galvanometer reaches zero again, and again *no* current

flows. Changes in the intensity of light will now be completely eliminated since the light reaching the cells has to pass through equally absorbing mediums (the tissue in the case of cell C_1 and the filters in the case of cell C_2) and the currents generated oppose and nullify each other. However, changes in the absorption due to changes in the volume of the finger, affecting cell C_1 only, will come through. Thus the angle of the deflection will be sufficiently small for a straight calibration line to be obtained and any change in the source of light will be nullified. *Fig.* 366 illustrates tracings obtained by this method.



FIG, 366.—Tracings obtained with the photo-electric plethysmograph described in *Fig.* 363. Second right finger (A) dilated and (B) in a constricted state. (Mr. E. J. H.). Room temperature 32° C. Time marks in B, 0·25 sec.

3. DI-ELECTROGRAPHIC METHOD

In 1932 Atzler and Lehmann[2] described a di-electrographic method for the registration of the cardiac activity which they suggested might be used also for limb plethysmography, as later communicated by Asher and Hopf.[1] The principle of the method is the following: Two oscillating circuits are tuned and the arm of the subject is brought into the field of a condenser of one of the circuits. The changes in the volume of the arm are transformed into changes in the capacity of the condenser. After transforming the frequency changes, they are recorded by means of an oscillograph, being first rectified and amplified.

This method, however, is too complicated to be used in the clinical laboratory, but is mentioned to complete the description of the possible approaches to the measure of the volume changes.

THE PLETHYSMOGRAM

The plethysmogram of a normal subject may show three different types of waves: (1) The volume pulse occurring simultaneously with each heart-beat; (2) The respiratory waves; and (3) Undulations occurring spontaneously and in no relation to either the respiration or the heart action. The latter group is only of

psychological interest (Lehmann,[27] Berger[4, 5]) and is another expression of the Traube-Hering waves of the blood-pressure.

For the interpretation of a plethysmographic record we have to be clear about the question as to what we are actually recording. We do not directly measure, as often stated, the width of the vessels, but the blood content of the organ, the latter being primarily a function of arterial supply and venous return. An increase in volume can therefore result either from an increased arterial inflow and unaltered venous outflow, or from a diminished venous return and unaltered arterial inflow. For the decrease in volume the contrary holds good. Since the blood does not escape from the blood-vessels under normal conditions, changes in the blood content can be taken as indication of the changes in diameter of the vascular bed of the organ under consideration. Usually the changes will be due to vascular reactions, but it has to be kept in mind that changes in heart output also will change the volume. During rest, however, the heart output can be taken as being constant. Since the blood content depends on the amount of blood in arteries, capillaries, and veins, and volume changes may be brought about by changes in the diameter of any one of them, the question arises as to which of these portions of the vascular tree is responsible for a given change in volume. For the solution of this question we have to keep in mind that two different criteria are furnished by the plethysmogram: (1) The volume pulses; and (2) Changes in the volume of the organ as a whole. The pulse volume represents the difference between the arterial inflow and the venous return during a single heart cycle. It is the result of the bigger arterial inflow during systole than diastole, the venous return being constant. The height of the volume pulse depends on the following factors: (1) The heart output per beat; (2) The resistance at the periphery; and (3) The viscosity of the blood. Since during rest the viscosity and the heart output will remain practically constant, the volume pulse will mainly depend upon the resistance of the periphery. The volume pulse, therefore, gives actually an indication of the state of the smaller arteries and arterioles; its height will be normally determined by the elasticity (tonus) of the arterial side of the vascular bed. This can be proved by many facts. The pulse of the normal individual increases in height after the application of heat and decreases by cold due to diminished or increased tone of the arteries. In arteriosclerosis of the smaller vessels the volume pulses are found to be very much diminished in height and changed in shape, while the blood-flow through the capillary bed may not be greatly disturbed, as proved by other tests. Thus the height of the volume pulses is an important factor in determining the state of the arterial side of the vascular tree.

Changes in the whole volume, however, can mainly be taken as being due to changes in the blood content of the capillary bed and the smaller veins, especially the venules. It is known by the investigation of Krogh[26] and Carrier[11] that normally in the capillaries, with systole and diastole, changes in the speed only of the blood-flow occur, and only in pathological conditions is a real capillary pulse traced, while in the smallest arteries, volume changes are met during systole and diastole.

For the investigation of peripheral vascular diseases, tests described elsewhere,* which have been employed in the investigation of the physiology of the peripheral circulation, are applied, and the evaluation of the results so obtained is compared

* Under preparation.

with the normal. As Saint[42] was able to demonstrate, the method is essential (1) in differentiating between functional and organic obstruction of the blood-flow of the limb, or in assessing the relative degrees of both in a mixed case. Therefore it is an important help in establishing (2) the correct diagnosis, and (3) the prognosis of these cases. At the same time, (4) it presents clear indications as to treatment. It could be demonstrated that pathological changes might even be recorded before any notable clinical manifestation could be detected.

Thus the method partly competes with skin temperature measurements. The plethysmographic record, however, is capable of furnishing much more detailed information about the state of the circulation in the area under consideration, and is always able to furnish results even when no changes in skin temperature can be traced.

SUMMARY

The guiding principle and the detail of construction of different types of plethysmographs have been given and the interpretation of the plethysmogram has been discussed. The application of the test employed to functional and organic vascular diseases will be dealt with in subsequent communications.

It is with pleasure that I put on record my indebtedness to Professor C. F. M. Saint of this Department for the interest taken in this work and his helpful criticism. I am indebted to Dr. C. B. O. Mohr (Department of Physics) for assistance in mathematical solutions. I should also like to thank Mr. E. J. Henderson, of this Department, for placing himself always at my disposal.

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PRECOCIOUS PUBERTY IN A BOY OF ONE YEAR

By IAN FRASER

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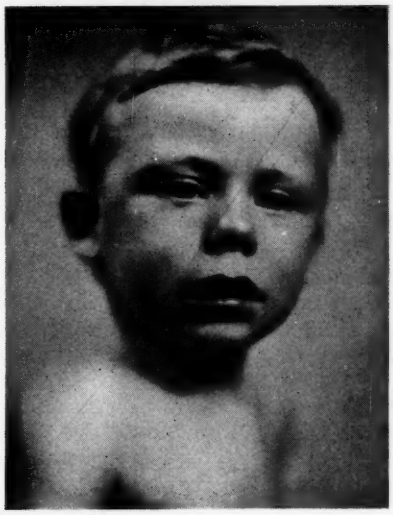
JUDGING by the small number of published cases, precocious puberty is a rare condition. As the disease is an interesting one, it is probable that most of the cases have been recorded. It seems to be found three or four times more frequently in girls than in boys; Kepler (Mayo Clinic) was able to collect from the literature only 37 cases in children, and of these 12 were in boys. Broster, in what is probably the most exhaustive survey of the subject, mentions only one case in a boy, so perhaps I may be excused if I give the details of what was to me a very interesting case of virilism—pubertas præcox, or precocious puberty—in a baby of twelve months.

CASE REPORT

HISTORY AND CLINICAL FEATURES.—Sammy (*Figs.* 367, 368) was first brought to my out-patient department when 12 months old. He was the only child of apparently healthy parents; his father was 27 years of age and his mother 28, and he was born 4½ years after



FIGS. 367, 368.—Sammy, aged 12 months.

their marriage. There had been no other children or miscarriages, and the family history on both sides for several generations back was negative of anything germane to this disease. Until the age of six months he was a normal child in every respect, when the following features rapidly began to appear. I have grouped them rather loosely into three groups—sexual, physical, and mental.

Sexual.—

1. The penis began to enlarge rapidly, and when first seen at the age of 12 months equalled in size that of a man of 18 years (*Fig.* 369).

2. The prostate became the size of a walnut—normally it is impossible to feel the prostate in a child of one year (*Fig.* 370).

3. Erections of the penis were almost constant.

4. Masturbation took place frequently. This, in fact, was one of the deciding factors in the child's being brought to hospital, as the mother was ashamed that when in public in her arms he always seemed to be rubbing his penis against her body.

5. Pubic hair appeared sparsely.

6. Acne of puberty appeared on the face.

Physical.—

1. Face became old for his age.

2. Voice became deep pitched.

3. Hands were very much enlarged.

4. Muscular development was excessive—it was almost impossible for his mother to control him.

5. Appearance of epiphyses was greatly in advance of his age. At one year of age he had five epiphysial centres in his carpus, as compared with the normal one or two. Other epiphyses were correspondingly advanced. (*Figs.* 371, 372.)

6. Body-weight increased out of all proportion—this was not to be wondered at, as the ward sister had to bring him three times the supply of food normally given to a child of his age.

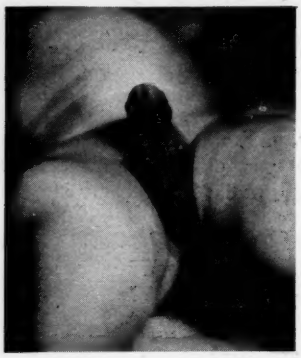


FIG. 369.—Genitalia at the age of 12 months.

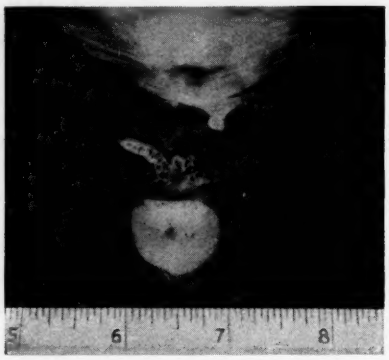


FIG. 370.—Prostate, seminal vesicles, and bladder (posterior aspect).

Mental.—

1. He was unable to talk, and rarely used the "Mama—Baba" words that one might expect of a child of 12 months.

2. He seemed to have little affection—except for food.

3. From six months on he lost his cleanly habits as regards urine and fæces.

4. He became bad tempered and difficult to manage.

I do not claim that these had any direct connexion with his increased virilism.

On presentation at my out-patient department at the age of 12 months, the above was the clinical picture, with the history of sudden onset at the age of six months and a rapid progress since. Briefly the boy's age was: (*a*) By calendar, 12 months; (*b*) By mental advancement, 12 months; (*c*) By bone epiphyses, 5 years; (*d*) By dentition, 3 years; (*e*) By sexual organs (penis and prostate, but not testicles), 18 years.

DIAGNOSIS.—The problem was: Where was the lesion? The suggested possibilities were: (1) Pineal; (2) Lesion in the region of the corpora mammillaria, floor of 3rd or 4th ventricle, or hypothalamic region; (3) Testicular; (4) Pituitary; (5) Adrenal cortex.

Clinical.—There was nothing to suggest an intracranial lesion; optic discs, radiographs, etc., were in every way normal. A true pituitary lesion causing virilism has not yet been found in a small child. As regards the testicles, an interesting feature was that although the penis was so large, yet the testicles were very small—almost smaller than those of a boy of 12 months. The probable cause was thus a lesion of the adrenal cortex, either hypertrophy, an adenoma, or a carcinoma; and with the history of normality until the age of six months and then a well-defined onset with rapid progress, the probability was adenoma or carcinoma. Definite diagnosis was difficult; abdominal palpation was negative—and untrustworthy in a fat boy. A straight X-ray photograph showed no shadow above the kidney shadow, nor did it show that the latter was depressed on either side. An intravenous uroselectan picture showed

normal renal pelves with no filling defect in the upper pole and no displacement of the kidney. It is generally considered that it is impossible for the upper renal calices to be deformed by an adrenal tumour, as there is such a good layer of kidney cortex, and, further, the adrenal gland is not so intimately connected to the kidney that it is not free to enlarge without encroaching upon the latter. One feels that this is a text-book statement based on theory rather than fact. No attempt was made to inject air into the perirenal tissue, as it is generally condemned in the literature as being of doubtful value, definitely dangerous, and a considerable hindrance to the ultimate operation.

Biological.—As clinical tests were thus of no definite value, the next step was to make use of biological methods, and I must here state my great indebtedness to Dr. Jocelyn Patterson, of Charing Cross Hospital Institute of Pathology. I was asked to forward two gallons

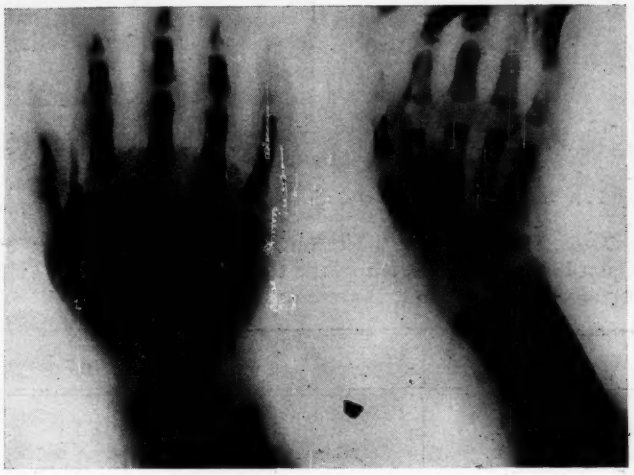


FIG. 371.—Radiograph of hand, with control of same age.

FIG. 372.—Radiograph of pelvis, with control of same age.

of the child's urine in a petrol can—this, I may say to those who have not tried it, is a rather arduous task considering that the untrained child of one year was passing his urine at irregular intervals and in small quantities into his napkin ! Two tests were carried out upon the urine. The first of these was a rapid calorimetric test of the urinary sterones, a test devised by Dr. Patterson ; the second was the biological assay, where a benzine extract was made of the urine after suitable acidification, and this with further treatment was injected into the pectoral muscles of caponized Brown Leghorns (*Fig.* 373). This work was done by Dr. Alan Greenwood, of Edinburgh. The Brown Leghorn is chosen apparently because its comb is more sensitive. Castration takes place at three weeks and the bird is usually not used till 40 weeks old, to make sure that no testicular tissue has been left behind undetected. Occasionally some are caponized as adults. The Plymouth Rock has been tried ; it is much easier to caponize, but requires three times the amount of stimulation. After injection the increase in the surface area of

the comb is measured (length by height). The increase to a known quantity of male hormone, meaured in international units, has already been recorded for that particular comb, and so the male hormone in the unknown urine can be estimated and the figure given in international units. The foundation of this work dates back to the year 1849, when the discovery was made by the Göttingen physiologist,

FIG. 373.—Capon, before and after treatment by male hormone.

Arnold Adolf Berthold (*Fig.* 374), that the comb growth was dependent, not upon nervous stimulation, but upon hormones produced in the testes.

The figures obtained for the two tests were as follows :—

	"SAMMY"	ADULT MALE	ADULT FEMALE	CHILD
Colorimetric— Sterone content (mg. per litre)	28	10–20	5–10	Trace
Biological— Male hormone content (i.u. per litre)	90	20–80	10–50	Trace

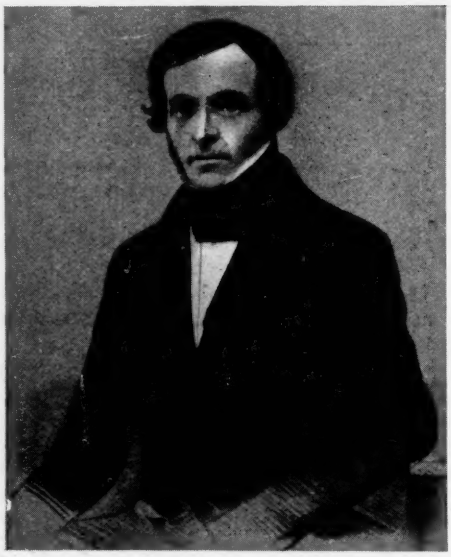


FIG. 374.—Arnold Adolf Berthold, Göttingen, 1849.

It will thus be seen that the small Sammy at twelve months of age was more virile than the average adult male.

OPERATION.—Operation was postponed for as long as possible. The child was felt to be a poor surgical risk and the reports of these cases in young children were very disheartening. Minor surgical adventures with the child had already given rise to great anxiety—e.g., circumcision, anæsthesia for intravenous pyelography, and tonsillectomy.

The first operation was an abdominal exploration, and at this a tumour the size of a golf ball was easily felt above the right kidney. Nothing could be felt on the left side. The rest of the abdominal contents felt normal.

After a considerable delay the second operation was performed. The boy was then 18 months old—that is six months after his first appearance at hospital. A high kidney incision was made. The twelfth rib was retracted and the tumour delivered with much greater ease and much less bleeding than was expected. The

tumour was pyriform, with the apex apparently attached without a stem to the inferior vena cava (*Fig.* 375). The child was back in bed in thirty minutes and later in the day he had recovered well and was taking fluids ravenously. Suddenly, twenty hours later, he collapsed and died. Cause?

POST-MORTEM EXAMINATION.—A complete autopsy was performed. The right adrenal bed was dry and normal. The left adrenal was found to be normal macroscopically and histologically (*Fig.* 376)—a suggested cause of death was absence of the other adrenal, which was now ruled out. The thymus gland was normal, although in these cases it is said to persist and to be abnormally large and is given as a cause of the

FIG. 375.—Tumour after removal (small fringe of original adrenal gland is visible).

so-frequent sudden post-operative deaths. The penis was as described, and the testes were very small and on section were found to be immature and without any signs of spermatogenesis (*Fig.* 377). Nothing was found in the pituitary, which was removed for section. The bladder, seminal vesicles, and prostate were removed *en bloc*. *Fig.* 370 shows the enlargement of the vesicles (until then unsuspected) and the prostate. These, taken in conjunction with the immature testes, are a point of great interest. The adrenal gland removed was as shown in *Fig.* 375; it weighed 37·05 g., and measured 2 × 1½ in. It was considerably larger than those cases of adrenal hypertrophy in adult females as described by Broster. There was a fine fringe

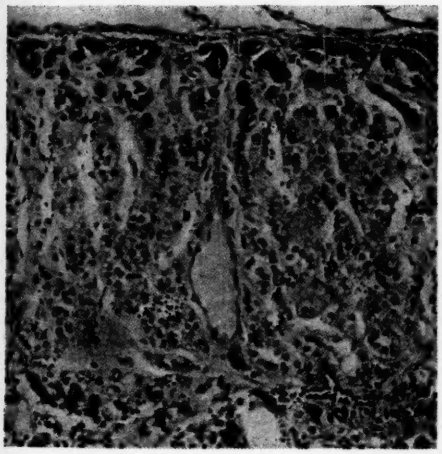


FIG. 376.—Left adrenal gland (normal).

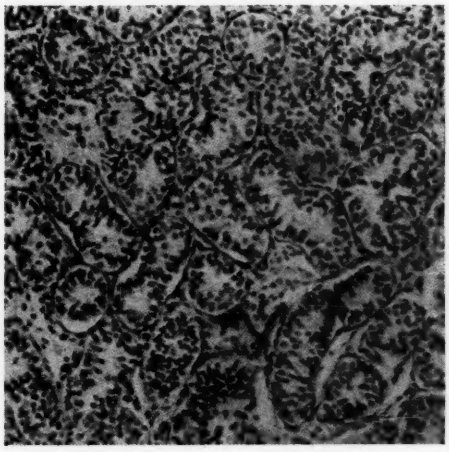


FIG. 377.—Testes. No sign of spermatogenesis.

of drawn-out adrenal gland, which ran along one edge of the tumour, whilst the latter itself was soft, diffluent, and felt almost fluctuating in parts. No attempt was made to test for the adrenogenic activity of an extract from the tumour. One was content to stain it with the ponceau fuchsine stain (Vines), which, as expected, was strongly positive (*Figs.* 378, 379).

FIG. 378.—Adrenal tumour. Positive ponceau fuchsine stain.

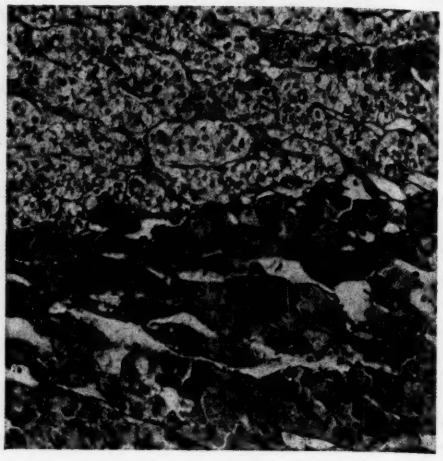


FIG. 379.—A case of virilism, for comparison, in which the gland showed a positive ponceau fuchsine stain, but in which there was also an adrenal adenoma which was negative to this stain. (*Professor Biggart.*)

SUMMARY

This is the case report of a boy of twelve months with extreme virilism. The points of interest are :—

1. It is one of the youngest cases on record.
2. The steps leading to the diagnosis are given.
3. The interesting relationship in virilism of the enlargement of the penis, prostate, seminal vesicles, and the absence of enlargement of the testicles, is shown.
4. Precocity in bone and dentition was noted (this latter has been denied by certain observers).
5. The value of the capon and colorimetric tests, as well as the ponceau fuchsine stain, is acknowledged.

I should like to express my thanks to Sammy's parents, who entrusted to me their only child in full confidence, and, although I failed, are still unable fully to express their gratitude.

I must thank Mr. L. R. Broster for his inspiration and guidance in what I found a difficult but absorbingly interesting case, Dr. Patterson for his generous help in the matter of urine examination, and my friend Professor Biggart, not only for his help in the histology of the case, but also for the stimulation which he gives to any work which aims at separating facts from fancies.

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CLOSED INTRAPLEURAL PNEUMOLYSIS*
AN ARTICULATED HOOK CAUTERY

By R. J. C. MAXWELL

The adhesions complicating artificial pneumothorax are complex and multiform structures; the cauterizing weapons of the thoracoscopist seem, by contrast, relatively simple. For the section of the great majority of divisible intrapleural adhesions, the loop cautery is the most suitable instrument. The original platinum loop cautery of Jacobaeus[1] has been modified by Unverricht,[2] Maurer,[3] Matson,[4] Chandler,[5] and others. Cova[6] was the first to employ a cautery with a hinged loop, which permitted perpendicular contact between adhesion and cautery whatever the position of the adhesion.

The loop cautery is not, however, the most suitable instrument for the division of all types of adhesion, and our armamentarium includes a cautery with a hook-like tip which fixes the adhesion and prevents it from slipping off the blade during cauterization. Saugmann[7] was the originator of this modification, which was later adopted by Jacobaeus.[8] The fixed-hook cautery is a useful instrument for dealing with adhesions arising from or lying on the mediastinum or on the superficial intercostal vessels of the paravertebral gutter. These can be caught with it and lifted away from their unsafe surroundings before division. Special operation tables for adhesion section have been designed by Kremer,[9] Gullbring,[10] and Viegener,[11, 12] which allow the patient to be placed in positions where the adhesions fall away from the mediastinum or posterior chest wall. Operators using these tables are still only a fortunate few, and we have in the hook a practicable—and less costly—solution of the problem presented by adhesions in close relationship with vascular structures.

When the adhesions to be cauterized are long and loose cords, on being lifted outwards they bend at the point of contact with the hook, which, when the current is turned on, becomes fixed in the corner thus formed and divides the adhesion there. If, however, the fixed hook is used for the cauterization of shorter and stouter cords or bands, the disadvantages of oblique contact between adhesion and cautery become apparent. These adhesions are tenser and bend less. No well-defined corner forms in which the hook can fix itself. As the angle between hook axis and the proximal part of the adhesion remains an acute one, the hot stem of the cautery runs obliquely across the lung end of the adhesion and may cauterize tuberculous foci or a cone of pulmonary parenchyma present in it (*Fig.* 374). Further, as division proceeds there is a tendency for the hook to travel lungwards away from the safely divisible fibrous part of the adhesion.

In an attempt to overcome these defects I had an articulated hook cautery constructed, in which a movable hook could be adjusted by a milled screw on the cautery handle to any angle with the shaft between 0° and 90°. When this cautery is employed the long axis of the hook can always be placed at right angles to the long

*From the King George V Sanatorium (London County Council), Godalming, Surrey.

FIG. 380.—Thoracoscopic view of an adhesion inserted on the neck of the first rib and first interspace to show how the stem of the fixed hook lies on the lung end of the adhesion.

FIG. 381.—Thoracoscopic view of a stout cord-like adhesion inserted on the first intercostal space, to show that only the cutting part of the blade of the hinged hook touches the adhesion. In this case the parietal expansion of the adhesion did not allow the hook to be placed far enough away from the lung for safe division in one stage, and the adhesion was divided in several bites nearer the chest wall.

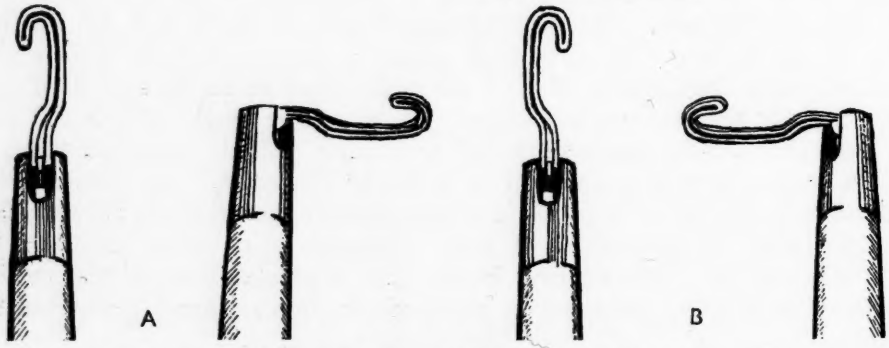

FIG. 382.—A, Left articulated hook in the straight and right-angled positions. This cautery is mainly used in right-sided pneumothoraces. B, Right articulated hook.

FIG. 383.—Thoracoscopic view of a loose cord inserted on the left superior intercostal artery and lying on that vessel and the subclavian artery. It has been lifted away with the hook. Note that the broad surface of the latter is used for coagulation. The retracted divided ends of a membrane can be seen in the foreground.

axis of the adhesion (*Figs.* 381, 382), thus avoiding injury to lung. In addition, the angled hook is never lost sight of, hidden from view by the shaft, as the fixed hook may be in some relationships of cautery and thoracoscope.

The articulated hook cautery has been employed at some stage in 40 (44 per cent) of the 90 operations performed since it has been in use. In 17 of these it was used for the division of more than one type of adhesion. Although this series of operations is small, it is large enough to give a general idea of the indications for the use of the articulated hook. It will be seen from the following list that the hook cautery has been found helpful in the cauterization of other types of adhesion in addition to apical and mediastinal cords :—

Loose cords and bands (apical, mediastinal, paravertebral, or vertebral) (*Fig.* 383)	30 cases
Vertical juxtavertebral sheets	10 ,,
Horizontal or oblique paravertebral membranes	4 ,,
Pillars (juxtavertebral or vertebral)	4 ,,
Membranes inserted on dome and mediastinum	5 ,,
Bands and cords near a cannula	2 ,,
Diaphragmatic adhesions	2 ,,

Vertical Juxtavertebral Sheets and Membranes.—The mediastinum is mobile to a greater or lesser degree in every case of artificial pneumothorax in which an effusion has not at some time occurred; it moves a varying distance—often some centimetres—towards the contralateral side when the patient assumes the

FIG. 384.—Thoracoscopic view of the posterior ends of the upper four ribs to show the posterior relations of a vertical membrane lying on the rib heads or vertebræ in this region. The first intercostal vein is seen running across the neck of the first rib towards the right innominate vein. The second, third, and fourth veins run downwards over the vertebræ before uniting to form the superior intercostal vein. The intercostal arteries are not visible.

FIG. 385.—Thoracoscopic view of a membrane inserted on the juxtavertebral region and pleural cupola which lies on the rib heads and vertebral bodies (cf. *Fig.* 384). The lower part was first thinned on the anterior surface, then divided with the hook; the upper thinner part was divided with the hook alone, as was a posterior horizontal limb which ran forward across the first dorsal vertebra.

lateral position generally adopted for the cauterization of adhesions. As the mediastinum carries the collapsed lung with it, vertical sheets or membranes inserted on, or in the vicinity of, the rib necks and heads, often lie so closely applied to the sides of the vertebral bodies and the intercostal vessels that complete division from the anterior surface is hazardous (*Figs.* 384, 385).

However, the desired line of section can be safely marked out on the anterior surface by a band of coagulation across it, and the thicker sheets reduced in bulk by partial division along this line. Division is then completed from the posterior surface of the membrane, and can be more conveniently completed with the angled hook. This is inserted under one free border of the sheet and divides it in a series of bites (*Fig.* 386). As the lower edge of a membrane is usually more accessible than the upper, a left-angled hook is required in right-sided cases and vice versa.

FIG. 386.—Thoracoscopic view of a vertical membrane attaching the posterior apical region of the right lower lobe to the sixth and seventh ribs in the costovertebral gutter. The adhesion has been thinned on the anterior surface near the chest wall, and division is being completed with the angled hook.

Paravertebral Bands and Membranes.—Medial to the angles of the ribs the intercostal vessels are separated from the pleural cavity only by a thin layer of parietal pleura. Paravertebral bands sometimes lie closely against these superficially running vessels. Rolling the patient forward on the operating-table may not materially improve the situation, and if division is completed from the anterior surface there is a considerable risk of injuring an intercostal vein. Four bands and four membranes of this type have been encountered. They can be more easily picked up and divided with the articulated hook cautery set at an angle of from 45° to 90° than with the angled loop cautery (*Fig.* 387).

A paravertebral band which is too bulky for the hook can usually be reduced to a suitable size by further anterior division with the loop cautery, but if this seems unsafe, the band is divided with the hook in a number of small bites. This piecemeal division is also useful for short bands with a fish-tail parietal insertion, in which the parietal expansion prevents the hook being held close to the chest wall and tends to slide it towards the thinner central part of the adhesion where division may be unsafe (*see Fig.* 381). By cauterizing the adhesion in several stages, division can be carried out close to the parietes.

FIG. 387.—Thoracoscopic view of a membrane between the right oblique interlobar fissure and the fifth rib, which has been divided from the scapular region backwards to the juxtavertebral region. The posterior border has been lifted away from the parietes and is being divided with the angled hook.

Pillars (Juxtavertebral and Vertebral).—Cylindrical or oval adhesions, the thickness of a finger or thumb, inserted on the necks or heads of the ribs or even on the bodies of the vertebræ, are not uncommon in the apical region. After division of the main mass the posterior

layer of the adhesion lies, as a thin sheet, closely against the ribs or vertebræ, and has to be divided from its posterior aspect. For this, the articulated hook is sometimes more convenient than the loop cautery. It has been used for four adhesions of this variety. The following case is an example :—

A long lung stalk, inserted on the first interspace and the neck of the second rib, with a poorly marked parietal expansion and an external fibrous portion only a few millimetres long, had been left untouched at a first-stage operation at which apical and lateral adhesions were divided. At the second stage a month later the fibrous part of the adhesion was found to be about three-quarters of a centimetre long. After preliminary paravertebral anæsthesia of the first and second intercostal spaces, the adhesion was divided from its anterior surface with the loop cautery hard against the chest wall by alternating diathermy coagulation and galvanic section. At the end an area of rib periosteum one centimetre in diameter lay exposed in the adhesion base. The loose posterior pleural layer was picked up from the heads of the ribs and divided with the angled hook. The febrile reaction (99·6° F.) lasted one day only. A small sinus effusion occurred, but disappeared within two weeks.

Membranes Inserted on the Pleural Dome or Mediastinum.—Loose membranes between the lung apex and pleural cupola are treated in much the same way as cords with similar attachments, being lifted away from the mediastinum with the hook, suitably angled, and divided in a varying number of bites according to their width. Membranes between the medial surface of the lung and the mediastinum are, even when long, more difficult to examine and cauterize, as the greater part of the adhesion is hidden by the overlapping upper lobe. The hook set at a right angle is invaluable here. It dips in between lung and mediastinum, lifts up the membrane bit by bit, and allows each portion of it to be carefully examined and, if safely cauterizable, divided.

These vertical mediastinal membranes can be divided much more easily and safely with the articulated hook than with any other type of cautery.

FIG. 388.—Thoracoscopic view of the division of strands near a cannula inserted in the third interspace in the mammary line. Some clear effusion is present in the gutter between lung and anterior chest wall.

Cords or Bands near a Cannula (*Fig.* 388).—Adhesions may be found so near a cannula that division with a fixed cautery from this cannula is difficult or impossible. If the instruments are interchanged the adhesion is so close to the lens window of the thoracoscope that a satisfactory view of it cannot be obtained. In the case of cords or bands withdrawal of the cannula and re-introduction in another interspace can be avoided by using the angled hook. The intrathoracic portion of the cannula is shortened to a few millimetres and the end of the cautery shaft introduced just beyond the end of the cannula. If the hook is now adjusted to a right angle any band within a radius of one centimetre can be picked up near the chest wall by a rotary movement of the cautery shaft.

In this series of operations hook division has been employed only for adhesions resting on or in the probable neighbourhood of blood-vessels. These seem to be

the correct indications for the hook divisions of adhesions, and, if they are strictly adhered to, it is obvious that only a small proportion of all cauterizable adhesions will require section with the hook. But many types of adhesion are usually present in the same pneumothorax, and it appears from this series of operations that hook division is indicated at some stage in approximately 44 per cent of adhesion section operations. I am convinced that in many of these cases division with the adjustable articulated hook is safer and easier than with the non-mobile hook cautery.

No instrument has been, or is likely to be, produced which will render the division of many of the intrapleural adhesions anything but difficult and tedious. The experience, skill, and patience of the operator will always be of greater importance than his equipment. But an instrument that will make even a limited number of these difficult operations a little easier, safer, and perhaps more complete, seems worth a place in our armamentarium.

SUMMARY

1. The indications for the hook-cautery division of intrapleural adhesions are discussed.

2. The limitations of the fixed hook are defined.

3. An adjustable articulated hook cautery is described.

4. A series of 40 operations, in the course of which this cautery was employed, is analysed. The adhesions cauterized are classified and special points in technique in dealing with certain groups are mentioned. The widened field for the hook division of adhesions presented by the articulated hook cautery is indicated.

I wish to thank the London County Council and Dr. James Watt, Medical Superintendent of the King George V Sanatorium, for permission to refer to the cases operated upon there. I am indebted to Mr. Schranz, of the Genito-Urinary Company, London, for the production of the cautery.

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REMNANTS OF THE VITELLINE VASCULAR SYSTEM AS A CAUSE OF INTESTINAL OBSTRUCTION

By J. SCOULER BUCHANAN and HENRY WAPSHAW, Glasgow

The two cases herewith recorded would appear to be of considerable interest on account of their embryological significance and of the rarity of the condition. It is often said in surgery that " things come in runs ", and this would seem to hold good here, as the two cases came under our care within two weeks of one another. We were fortunate, also, in finding that, while the vitelline vascular system was implicated in both, the venous remnant was at fault in the one and the arterial in the other.

Aberrant derivatives of the omphalomesenteric tract, with their attending complications, have prompted numerous contributions to the past and present literature, and we can no longer look upon these vagaries as being scarce. Yet it seems strange that such anomalies should be mainly related to the ductal element of the vitelline system, and that so little importance should be ascribed to the vascular elements, in the absence of any failure in yolk-duct retrogression or intestinal development. The explanation of this incidental bias must be their rarity, although their existence was, none the less, well known to Meckel.

With so few recorded cases of this singular vascular aberration, it is unjustifiable to draw conclusions, but it may be stated, with some degree of certainty, that the arterial remains show a higher incidence than the venous. This opinion would seem to be further supported by the not infrequent occurrence of a Meckel's diverticulum associated with a short mesentery, for the superior mesenteric artery, which supplies it, is a homologue of the vitelline artery.

The two cases presently reported are considered to be developmental errors which have resulted from imperfect recession of the omphalomesenteric vessels. Before proceeding, however, to an analysis of their nature, it is necessary to make reference to the normal fate of these fœtal structures.

EMBRYOLOGY

Vitelline Vein.—From the widespread venous ramifications on the yolk sac the vitelline vein is formed. This accompanies the omphalomesenteric duct proximally, till the latter merges with the apex of the exomphalonic midgut loop. It thereafter courses up in the ventral mesentery, through the infraduodenal region, where it divides to form the right and left vitelline veins, which terminate in the sinus venosus. Thus the nutriment of the yolk sac is carried to the heart, and redistributed by the heart to the embryonic tissues and the yolk sac.

The duodenum rapidly develops now, and its loop protrudes between the right and left vein, so that, when it, together with the stomach, swings to the right, the right vein passes posteriorly and the left anteriorly to the third part of the duodenum (*Fig.* 389).

The next stage is characterized by the selective disappearance and coalescence of certain parts of the venous plexus. Firstly, the right vein largely degenerates, after supplying a small tributary to the left one, and the latter is further supplemented by the confluence of the superior mesenteric vein, which is endogenous to the midgut mesentery; in addition, union with the splenic vein is established. The product of this fusion is the portal vein, which passes in the mesoduodenum, superficial to the third part and deep to the first part of the bowel, upwards to the liver. Frazer[1] states that the definitive portal drainage, with its tributaries, though rudimentary, is established and complete at a very early period, through the vitelline arrangements at the duodenum and liver.

Keith[2] points out that the three tributaries of the portal vein—the splenic vein from the foregut, the superior mesenteric vein from the midgut, and the inferior

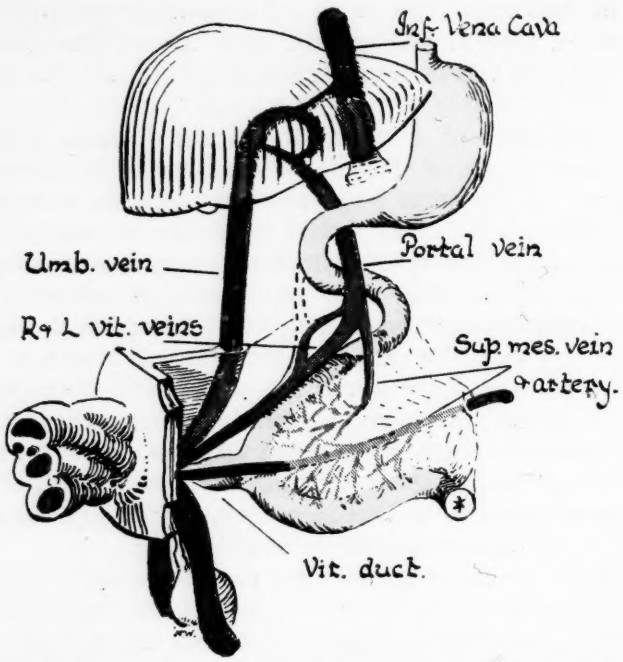

FIG. 389.—Normal transmutation of the vitelline vascular system to its ultimate fate, showing obliteration of the right and persistence of the left vein (blue). The vitelline artery (red) and its relationship with the superior mesenteric artery are also shown.

mesenteric vein from the hindgut—lie in the dorsal mesentery, while the terminal parts of the vitelline veins are situated in the ventral mesentery of the foregut.

After the sixth week, when the vitelline duct atrophies, the vein also becomes dissociated from the umbilical region, and forms a fibrosed vestigial strand, hanging from its place of attachment at the mesoduodenum, about the head of the pancreas —the exact time and method of disappearance are not definitely known (Frazer[1])— but should it fail to disappear, the result is an intraperitoneal band, which connects the navel to the vicinity of the head of the pancreas. One might speculate that the reverse may occur, and thus leave the remnant still attached to the umbilical region, but free from its mesoduodenal attachment. Such remnants, in exceptional circumstances, contain a patent vessel.

Vitelline Artery.—The ultimate differentiation of the arterial component is less complex, but the same view cannot be held of its genesis. At the early stage of the embryo, the three cardinal alimentary arteries, the cœliac axis, the superior mesenteric artery, and the inferior mesenteric artery, are represented by right and left branches, arising from the corresponding stems of the paired aortæ. When the stems coalesce, a fusion of their main branches probably also occurs, but this hypothesis has not been fully substantiated by embryologists. Frazer, whose authority we herewith cite, further states: "Little appears to be known about the isolation of the three large branches, and their changes of level in accordance with the changes of the viscera".

Nevertheless the vitelline artery may be considered the continuation of the superior mesenteric artery, accompanying the vein and the duct to the yolk sac, where it ramifies widely. It disappears at an earlier period than the vein, but, if retrogression be incomplete, the residuum is a fibrous cord extending from the mesentery of the terminal ileum, about the site of the occurrence of Meckel's diverticulum—i.e., the apex of the midgut loop—to the umbilicus, but variations may occur as to the method of disappearance, similar to those already described in the case of the vitelline vein.

COMPARATIVE ANATOMY

It is interesting to discover that, just as Ruysch[3] was acquainted with the diverticular vestige of the vitelline duct a century before it was christened with its now familiar designation, so the earliest record of the existence of vitelline vessels in lower animals was made by Blasius[4] about the latter part of the seventeenth century. However, it is to Meckel,[5] Schroeder,[6] and Allen[7] that we owe the elucidation of the comparative anatomy of the problem. They stated that legacies of this vascular system are a common occurrence in the newly-born of certain animals. Thus Schroeder found fibrous cords in a high percentage of dogs, kittens, and rabbits; Allen's work concerned dogs, kittens, guinea-pigs, and rabbits, and he described, examining the first two species, twin bands—(*a*) one extending from the umbilicus to the mesentery near the lower ileum, and (*b*) one extending from the umbilicus into the mesoduodenum, and terminating close to the pancreatic lobes. He concluded that the former was an arterial, and the latter a venous, derivative. In rabbits he could detect only one band, which passed from the navel to the portal vein, and obviously belonged to the latter group.

LITERATURE

In his classical expositions of ileo-umbilical developmental errors, Meckel contributed much information about the subject under consideration. He described a case of a child, aged 3 months, with a vascularized cord passing from the superior mesenteric vein and artery, which after running along the diverticulum (i.e., Meckel's), hung free therefrom as a solid thread in the abdomen. He quoted certain of his predecessors, who had recorded similar threads, unattended by congenital appendages, which had become glued to odd sites in the peritoneal cavity, and he emphasized their potential danger. Meckel substantiated the vascular origin of these structures from a study of intact vitelline remains in human embryos older than ten weeks, and those of certain carnivora; he concluded that they disappeared later than the yolk duct.

Subsequent authorities (Leichenstern,[8] Forster,[9] etc.) cast a certain amount of doubt on the developmental origin of these abnormalities, which they regarded rather as post-inflammatory. Fitz,[10] however, in his illuminating and comprehensive survey of this region of embryology, furnished strong support for Meckel's views, although he admitted that a systematic search for vascular remains met with indifferent success.

Spangenberg[11] found, at a post-mortem examination on a youth, a vitelline vessel which passed backwards from the umbilicus, between the coils of intestine, till it reached the left of the spine at the mesenteric root, where it " emptied into a bifurcation of the superior mesenteric vein ". This was patent from its deeper relation to within two inches from the navel, and the histological appearance appearance resembled that of a normal vein.

King, [12] Mohamed,[13] Noaes and Hermeto,[14] and a few others have recorded cases of intestinal obstruction caused by bands of vascular derivation. Mohamed's case merits a detailed description. A youth aged 18 had succumbed to the obstruction, and at the autopsy a patent artery was found, which began at a point midway between the umbilicus and the symphysis pubis, and passed to the right iliac fossa to form a noose round a terminal ileal loop ; it finally continued towards the mesentery about three feet from the ileocolic artery. The fate of the parietal end was also interesting, in that it divided into two, one branch ascending to the umbilicus, the other fusing with the left superior vesical artery.

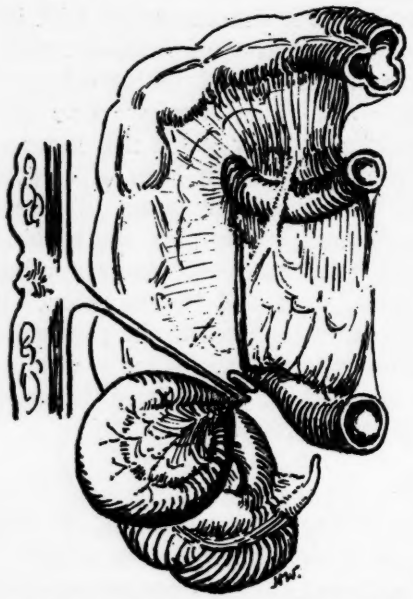

FIG. 390.—*Case* 1. Persistence of the right vitelline vein disappearing below the third part of the duodenum, after having ensnared a loop of the small bowel.

It has been frequently noted, according to Cullen,[15] that, when umbilical polyps are being removed, a vessel spurts, and he believed that this was undoubtedly a patent omphalomesenteric artery. Fraser and McCartney's[16] case is of outstanding interesting in this connexion. They found a cord adherent to the peritoneal aspect of an umbilical polyp and to the mesentery of the lower ileum of an infant; at the latter fixed point an extravasation was seen, due to the disruption of the anastomosis between the cord and an arcade of the superior mesenteric artery.

CASE REPORTS

Case 1.—C. H., male, aged 20 years, was admitted to the Western Infirmary, Glasgow, on January 19, 1936.

HISTORY.—Four days prior to admission, he was suddenly seized with acute abdominal pain, following a normal stool. The pain was of a colicky nature and at times excessive. Vomiting supervened early and persisted, together with pain, until admission to hospital. The vomitus had become malodorous and fæcal in character. The bowels had not moved since the onset of the pain, and no flatus had been passed. Urinary retention had been present for ten hours prior to admission.

PAST HISTORY.—During the previous year he had had two similar attacks, transitory and of lesser intensity. There was no history of abdominal pain or crisis in childhood.

ON EXAMINATION.—Temperature 99·6°. Pulse 92 per minute. The patient was obviously extremely ill, and with a pinched and haggard expression. Some cyanosis was present. The tongue was dry and coated, and the breath was foul. The abdomen was greatly distended, especially centrally, and very tense. On abdominal auscultation, high-pitched tinkling was audible. On rectal examination marked ballooning was present. The heart-sounds were poor and the pulse was easily compressible. Numerous moist rales were present at both lung bases.

It was evident that the patient was suffering from an acute intestinal obstruction, probably of the small bowel.

OPERATION (J. S. B.).—After gastric lavage and intravenous saline administration, his condition improved somewhat, and it was decided to risk carrying out a laparotomy.

On opening the abdomen by a paramedian incision, the small bowel was found enormously distended, discoloured but viable. The obstructive element proved to be a stout plum-coloured cord originating in the parietes, in the neighbourhood of the umbilicus, and passing down towards the pelvis, twice encircling a loop of ileum, and causing an acute closed-loop obstruction. Thereafter it passed upwards on the surface of the mesentery, to disappear retroperitoneally *below* the third part of the duodenum (*Fig.* 390). Owing to the critical condition of the patient, further investigation regarding the orientation of the cord was precluded. The cord was removed and the obstruction relieved, and the wall of the bowel at the stricture being definitely viable, the abdomen was closed.

Examination of the cord removed showed that it was 8 in. in length, and tapered from ½ in. at one end to ¼ in. at the other (*Fig.* 391).

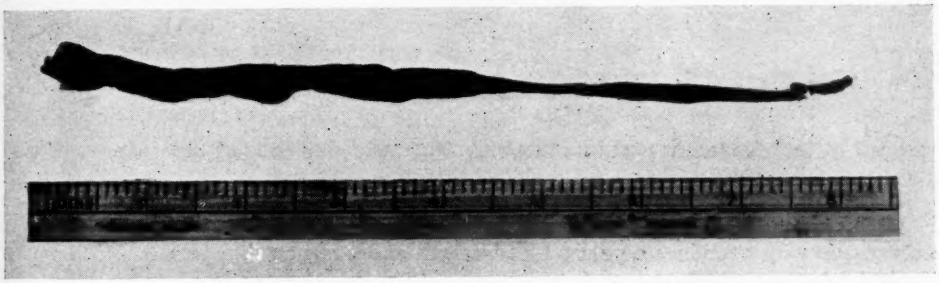

FIG. 391.—*Case* 1. Photograph of specimen.

POST-OPERATIVE COURSE.—For three days the patient improved and the bowels acted well. On the fourth, the abdomen became somewhat distended, and vomiting supervened. At the same time, the lung and heart condition worsened, and death occurred on the fifth day after operation. Unfortunately a post-mortem examination was not permitted.

HISTOLOGICAL EXAMINATION.—The specimen consisted of vascular fatty areolar tissue. Massive extravasation of erythrocytes into the tissue had occurred. Apart from three thick-walled veins, no structures suggestive of fœtal remains were found.

Case 2.—A. C., schoolboy, aged 12 years, was admitted on January 6, 1936, to the Western Infirmary, Glasgow, with a diagnosis of chronic appendicitis.

HISTORY.—For three months the patient had suffered from intermittent attacks of colicky abdominal pains, coming on at intervals of about three weeks. These would appear suddenly, and usually pass off in an hour or so. Although the colic was most intense in the right lower quadrant, it was sometimes located in the region of the umbilicus. The spasms gradually became more frequent and commanding, and were attended by vomiting and anorexia. There was an accompanying intestinal irregularity, the tendency being towards constipation; but two months previously he had been troubled with diarrhœa, which, however, did not persist. Previous health good.

ON EXAMINATION.—The patient looked a well-built and healthy boy, but his tongue was furred and his breath was offensive. The temperature was 99·8°, the respirations 22, and the pulse 120. The respiratory excursion of the abdomen was unimpaired; on palpation generalized tenderness was elicited, but mainly in the right iliac fossa—and unaccompanied

by muscular guarding. Otherwise, no abnormalities were found in the remaining systems, and no threadworms were found in the stools. The history seemed to indicate, from the nature of the pains, that some intermittent obstructive lesion was the cause of his complaint.

OPERATION (J. S. B.).—On January 10, 1936, laparotomy was performed, and in view of the obscurity of the diagnosis, the right paramedian approach was chosen. Exploration revealed a string-like band, which ran from the region of the umbilicus, where it was substantially anchored, to be inserted on the upper surface of the mesentery of the ileum about one foot from the ileocæcal angle (*Fig.* 392). It was about 4 in. long, and its calibre varied from a rather filamentous strand at its parietal attachment to about $\frac{1}{8}$ in. diameter at its mesenteric extremity. It was removed in its entirety. When attention was then directed to the appendix,

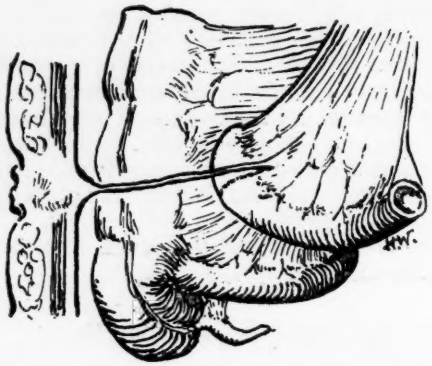

FIG. 392.—*Case* 2. Remnant of the vitelline artery, attached at umbilicus and upper surface of mesentery.

it seemed to be an innocent partner outwardly, but its section showed the presence of two or three small threadworms.

Recovery was complete and uneventful.

HISTOLOGICAL FEATURES.—The band from the abdomen showed the presence of fibro-areolar tissue with abundant capillary blood-vessels and a few small arteries. No remnant of intestinal structure was found.

ANALYSIS OF OUR CASES

In *Case* 1 (*Fig.* 390) the obstructing band appears to be clearly of venous origin, but its proximal place of attachment, adjoining the infraduodenal region, does not conform to the site usually described by embryologists, i.e., coursing over the third part of the duodenum towards the pancreas. This, however, may be explained in two ways :—

Firstly, it is possible that, while the distal end had remained fixed to the umbilicus, the proximal end had freed itself from its attachment about the head of the pancreas, but soon afterwards it became adherent to the mesenteric root.

Secondly, instead of conforming to what would appear to be the usual fate of the veins—namely, persistence of the left and disappearance of the right—the reverse occurred in the case now reported.

In *Case* 2 (*Fig.* 392) there would seem to be little doubt that the remnant was that of the vitelline artery. Its insertion into the mesentery and probable connection with a branch of the superior mesenteric artery conform to the accepted embryology of the structure. As in examples already cited in the literature, it would seem that in this case the cord very nearly succeeded in freeing itself from its umbilical attachment, to be left dangling from the mesentery.

SUMMARY

1. Two cases of small-bowel obstruction are recorded: the first case was one of acute strangulation as a result of the persistence of the right vitelline vein; the second, intermittent in type, was caused by a remnant of the vitelline artery.

2. The relative embryology and morphology are discussed, and the historical literature is summarily reviewed.

Our thanks are due to Professor Archibald Young for his permission to record these cases. To him and to Professor D. M. Blair we are further indebted for their help in the preparation of this paper, also to Dr. Janet S. F. Niven for carrying out the histological examination of the specimens.

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TRANSPLANTATION OF THE URETERS INTO THE LARGE BOWEL AND ITS EFFECT UPON THE KIDNEYS

By CLIFFORD MORSON and WILLIAM H. GRAHAM, London

The transplantation of ureters into the large bowel has become in recent years a recognized and justifiable surgical procedure. The names of Stiles of Edinburgh, Peters of Canada, and Coffey of America, will be always associated with the pioneer work which has converted this operation from an experiment to a practical proposition.

In this country during recent years Grey Turner, Henry Wade, and Bernard Ward have led the way in proving that the functional results are compatible with many years of good health and an absence of disability. The writings of these three investigators in particular have led us to study certain aspects of technique, and the physiological processes which arise from adapting a portion of large bowel as a substitute for the urinary bladder. All the cases which we have selected for the operation and subsequent investigations were those in which life had become intolerable owing to either bladder pain or dysfunction.

The most striking feature in our series of cases with regard to the immediate results is that no deaths occurred among the non-malignant cases, whereas the mortality-rate for patients suffering from cancer was extremely high.

Henry Wade has stressed this phenomenon in numerous writings on the subject, and in descriptive language refers to the "subtle poison" which in these cases thwarts the efforts of the surgeon. Frank Hinman's mortality figures are 50 per cent for cancer and 20 per cent for all others.

We are impressed with the low vitality of the ureter in the malignant bladder. Its blood-supply is subnormal, and even when the duct is only slightly dilated its tissues are friable. In our series the malignant disease has been advanced, and therefore the pain and hæmorrhage which it had caused over a long period was chiefly responsible for the devitalization of the tissues. It is quite possible that the death-rate would be considerably reduced if early cases of bladder cancer were selected for ureteric transplantation.

TECHNIQUE AND MANAGEMENT

Pre-operative Technique.—Hinman, of San Francisco, has given a detailed account of the various techniques which have been practised for diverting the flow of urine from the bladder. It is not our intention to give an historical account of the evolution of this operation: suffice it to say that in the initial efforts of one of us (C. M.) the recommendations of Coffey were adopted, but soon abandoned. We are satisfied that the use of indwelling ureteric catheters for draining the urine from the kidneys into the bowel during the first week after operation is a mistake. In fact we go so far as to state that not even a catgut suture such as is advocated by Mayo should be left in the lumen of the ureter. Any foreign body of whatever material which may be retained in the ureter acts as an irritant and obstructs the

flow of urine. Also the practice of fixing a tube in the rectum to allow of the escape of urine from the bowel for the first few days following transplantation of the ureters is of questionable value. Most patients dislike its presence intensely. We agree with Hinman that the best results are obtained with the simplest technique.

The most careful pre-operative preparation is essential in order to avoid urinary infection. It is our practice to give a colon washout each day for ten days; on the first and sixth of the days during this period an aperient is prescribed in order to empty the whole of the large bowel. It is not always easy to achieve this, but it is essential to the success of the operation. As a prophylactic against pyelonephritis sulphonamide in doses of $7\frac{1}{2}$ gr. is given three times daily for four days immediately preceding the operation. An excretion pyelography during this period is carried out in order to check the resultant changes in the kidney pelves.

Operative Technique.—General anaesthesia—gas, oxygen, ether—was employed in all cases. Unless the operation was to be performed for a vesicovaginal fistula, the bladder was emptied by catheterization as soon as the patient was placed on the operating table. In the extreme Trendelenburg position the abdomen is opened, the incision being made from the umbilicus to the pubes; the pouch of Douglas is cleared of small intestine and transverse colon, with the aid of a special self-retaining retractor which has been made for us by the Genito-Urinary Manufacturing Co. By the use of this instrument the assistant is free to help the surgeon with the more delicate part of the technique.

An incision is made in the peritoneum along the line of the ureter from a point below the sacro-iliac joint to the base of the bladder. The ureter is easily recognized by the presence of small vessels lying on its surface. The pelvic portion of the duct is then freed from the bed of cellular tissue in which it lies, to the point where it enters the wall of the bladder. Before dividing the ureter as it enters the bladder wall a special clamp is placed an inch or two above the point of division in order to prevent soiling the peritoneum by urine. A Souttar's needle is now passed through the proximal end of the ureter and a portion of its wall is tied with catgut. Ligation of the distal stump follows, together with the sewing of the peritoneum over the bed of the duct. The insertion of the ureter into the pelvic colon must be carried out with meticulous care, for it is in this part of the operation that an error in technique may produce fatal complications. The part of the pelvic colon chosen for the transplantation should be as near to the promontory of the sacrum as possible and where the bowel would lie with the patient in the erect position; thus there is no danger of kinking of the ureter and a minimum of tension.

The technique of the transplantation is that recommended by Wade, with certain slight differences. These are, that the Mayo stitch is not used, and on the left side the ureter is not passed through a hole in the mesentery before being inserted into the colon. No catheter is inserted into the ureter. An incision about two inches long is made in the peritoneal coat of the bowel and the peritoneum on either side of it separated from the muscle layer. The colon must be kept on the stretch while this is being done. A stab cut is made in the muscle coat and mucous membrane at the distal end of the two-inch incision, and through this the ureter, together with a Souttar needle, is passed into the lumen of the bowel. It is important to pull about an inch of the duct into the bowel before fixing it with the aid of the Souttar needle. The latter is brought out through all the coats and the catgut suture then tied.

The surgeon now proceeds to bury the ureter beneath the peritoneal coat of the large intestine. It is advisable to apply two lines of sutures to ensure that there shall be neither leakage of urine nor alteration in the desired position of the ureter. It is our practice to transplant both ureters at the same operation. It is also our custom to drain the pouch of Douglas by a small rubber tube for two or three days. The abdominal wound is closed in the usual way. Before the patient is returned to bed a tube is passed about three inches into the rectum and fixed to the thigh.

Post-operative Treatment.—The rectal tube is allowed to drain into a suitable receptacle for about five days, but it frequently causes discomfort, due either to rectal intolerance or to external pressure against bony prominences. In several cases, owing to the discomfort produced by this tube, it has been removed within forty-eight hours without any untoward results. It is doubtful whether the presence of the tube serves any useful purpose.

A solution of sodium sulphate, 3·4 per cent, is administered by intravenous drip immediately the patient has been returned to bed, and this is continued for forty-eight hours, being given at the rate of twenty drops per minute during alternate hours. We believe this to be a very important part of the post-operative treatment, for the sodium sulphate solution stimulates diuresis. Further diuresis is obtained by encouraging the patient to drink copiously. During the healing of the wound no aperients are given, any abdominal discomfort or distension being relieved by a small rectal washout on the third or fourth day. The suprapubic drain is removed in forty-eight hours. The patient is allowed to sit up on the eleventh or twelfth day.

Immediate Results of Operation.—Very little reaction or shock was shown in any of our cases. As a rule no urine was drained from the rectal tube until some thirty-six hours after the operation. This, we believe, is due to mechanical obstruction at the site of anastomosis. At the end of this time urine is excreted rapidly and in increasing volume. After the first five days convalescence is apyrexial. Several patients on removal of the rectal tube immediately had complete control. The others developed it in from twenty-four to forty-eight hours.

Frequency of bowel action after removal of the tube varied considerably. Most cases at first had hourly frequency, but the intervals rapidly lengthened and within three days of taking out the tube a bowel action occurred every two or three hours during the day and about the same number of times at night. All cases became continent within ten days of operation. At the end of this period, in addition to continency, most of the patients developed such control that they could discriminate between the expulsion of fluid, fæces, and flatus. Occasionally during the passage of flatus a little urine would be passed. After fourteen days each patient was able to control the bowel contents for three to five hours during the day. At night some had no actions, others had at most one or two. Only two cases developed pain or tenderness in the loin. This was not a marked feature in the convalescence of these two patients, the pain subsiding in two or three days after its onset. This sign in both cases appeared three days after operation.

The majority of patients were discharged from hospital at the end of the fourth week.

Pyelography.—As a routine, intravenous pyelography was carried out during the third week of convalescence. The pyelograms have shown that all normal kidneys develop a degree of hydronephrosis, the extent of the dilatation apparently being dependent upon the amount of obstruction produced in the ureter at the point of

anastomosis. In our later cases, as a result of increased experience of the technique, the immediate changes due to back pressure have been less pronounced. We are convinced that these changes in the kidney are due to mechanical causes and not to inflammation, on account of the fact that there is an absence of much constitutional disturbance such as prolonged fever and loin pain. Therefore the degree of temporary hydronephrosis is controlled by the technique of insertion of the ureters into the bowel.

A pre-operative hydronephrosis due to a growth of the bladder or narrowing in the intramural portion of the ureter subsides in less than a month after ureteric transplantation. This change is due, of course, to the relief from a prolonged pre-existing obstruction.

In all our cases intravenous pyelography is repeated six months later. It is then found that the degree of hydronephrosis produced by the operation has gradually subsided, although a pyelogram shows that the kidney does not completely return to its normal size. At the end of this period contraction of pre-existing hydronephroses is noticeable. This observation reveals the fact that on the removal of a mechanical obstruction which produces hydronephrosis the involution of the dilated pelvis and calices will occur without the necessity for any plastic operation upon the kidney itself.

RESULTS

Since 1936 13 cases have been submitted to ureteric transplantation into the pelvic colon for the following conditions :—

Tuberculous bladder	1
Carcinoma of the bladder	6
Carcinoma of the cervix, with invasion of the trigone	1
Complete procidentia, with vesical calculi	1
Complete incontinence	2
Systolic bladder due to chronic sepsis	1
Vesicovaginal fistula due to carcinoma of the cervix and vagina	1

Amongst these there were 5 deaths, 4 of whom had malignant disease of the bladder and 1 secondary invasion of the trigone, the primary lesion being in the cervix. Thus it will be noted that it was only patients with cancer who succumbed to the effects of the operation.

The most striking case of all in our series was a woman with complete procidentia, carcinomatous ulcers of the vagina, and a bladder full of stones. The malignant ulcers of the vagina caused numerous hæmorrhages, and death would have been inevitable had she not submitted herself to ureteric transplantation.

The notes of all these cases are recorded in detail, and some of them are illustrated by their pyelograms.

NOTES ON FATAL CASES

J. H., male, aged 57 years, was admitted to hospital in August, 1937, with a history of pain and frequency of micturition for two months.

Cystoscopy showed a large carcinomatous growth involving the base of bladder, especially on the right side. Per rectum the growth could be felt invading the prostate.

August 25, 1937 : Operation : Ureteric transplantation by the usual technique into the pelvic colon. The walls of the ureters were thickened and the lumens dilated.

August 26, 1937 : Urine is being passed per rectum.

August 27, 1937: The lower half of the abdomen is slightly distended and tender, especially on the left side. Urine still draining well per rectum. Patient very restless, and during night got out of bed.

August 28, 1937: Died.

POST-MORTEM EXAMINATION.—Malignant growth of bladder, pelvic peritonitis, and pyelonephritis. Right ureter had separated from bowel at point of anastomosis.

Comment.—The growth of the bladder was too far advanced even for ureteric transplantation.

H. F., male, aged 61 years, admitted to hospital in September, 1938, on account of hæmaturia and frequency and difficulty of micturition.

Cystoscopy showed the presence of an extensive carcinomatous growth surrounding the internal meatus and spreading up the right lateral wall of the bladder. Excretion pyelography: good excretion from both sides, indefinite clubbing of calices on the right side, but no other abnormality demonstrated.

September 23, 1938: The bladder was opened with the object of performing partial cystectomy, but this was found impracticable on account of the extensive involvement of the internal meatus. A cystotomy was therefore performed.

October 13, 1938: The ureters were transplanted by the usual technique into the pelvic colon; marked peri-ureteritis on the left side, right ureter dilated. The upper part of the pelvic colon was fixed to the left side of the pelvis, necessitating mobilization by incision of the lateral peritoneum.

October 14, 1938: No drainage per rectum.

October 15, 1938: Urine now escaping by rectal tube.

October 16, 1938: Has developed a cough, some collapse at base of left lung.

October 18, 1938: Abdominal wall has burst open, sutured under local anæsthesia.

October 19, 1938: Patient died.

Comment.—The post-operative convalescence demonstrated that the patient was not in a fit state to be submitted to ureteric transplantation.

G. H., male, aged 63 years. There was a history of pain on micturition and hæmaturia for four months. Suprapubic cystotomy performed at another hospital in October, 1937. Now has repeated attacks of hæmorrhage from the bladder and much pain.

March 21, 1938: Bladder explored through suprapubic opening and extensive carcinoma of bladder found. Transplantation of ureters into pelvic colon by the usual technique. Both ureters dilated and thin-walled. During the next twenty-four hours 44 oz. of urine passed per rectum.

March 22, 1938: Patient died quite suddenly the next day.

POST-MORTEM EXAMINATION.—It was found that there was a most extensive carcinoma of the bladder, chronic inflammation of the left kidney, and œdema and atrophy of the myocardium. There was no peritonitis.

Comment.—Owing to the patient's weak state, with so extensive a growth of the bladder complicated by severe attacks of hæmorrhage, it was an error of judgement to have performed an operation in this case.

I. H., female, aged 49 years. Four months' history of treatment by radium and X rays for carcinoma of cervix. Now has a vesicovaginal fistula.

Cystoscopy shows marked invasion of the bladder trigone.

October 13, 1938: Operation: Transplantation of ureters into pelvic colon. Both ureters dilated to the size of an infant's small intestine. A suprapubic drain was inserted. During the next twenty-four hours patient passed only 8 oz. in all through the rectal tube. Urine then commenced to pass through suprapubic tube, and death took place a day later.

Comment.—Owing to the devitalization of the tissues of both ureters due to irradiation therapy, sloughing took place at the point of insertion of the ducts into the bowel, and in consequence the patient died of peritonitis.

NOTES ON SUCCESSFUL CASES

J. W., female, aged 54 years. *Past history*: Cholecystectomy, 1933. December, 1935, treated with diathermy for carcinoma of bladder, which responded favourably, but she failed to return for further treatment. *Present illness*: Incomplete retention of urine. Bladder distended to umbilicus: 5-minute frequency of micturition by day and night.

October 16, 1936: Cystoscopy: Large carcinoma involving whole trigone and spreading to left side of bladder.

October 26, 1936: Excretion pyelography (*Fig.* 393). Right side, normal pyelogram. Left side, large kidney, regular dilatation with clubbing of calices; ureter also dilated and limbed at upper end. There is a filling defect of the bladder.

November 5, 1936: Operation: Both ureters transplanted into pelvic colon.

November 7, 1936: Patient stood operation well, no excretion of urine from rectum until this day, when 8 oz. of offensive and blood-stained urine were passed.

November 8, 1936: Patient has passed 42 oz. per rectum.

FIG. 393.—J. W., female, aged 54. Excretion pyelogram before ureteric transplantation into bowel. Left kidney is hydronephrotic, due to obstruction of the lower end of the ureter by the bladder growth.

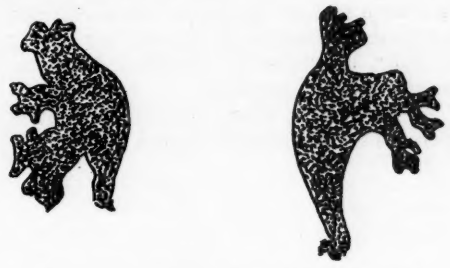

FIG. 394.—Same case, three weeks after ureteric transplantation. Right kidney is hydronephrotic, while there is little change in the left kidney.

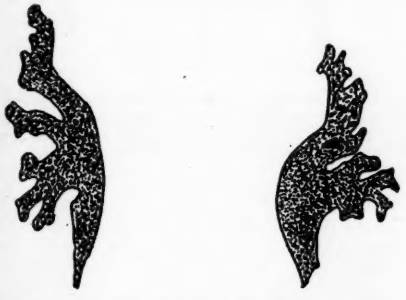

FIG. 395.—Eleven weeks after operation. The calices and pelves of both kidneys are less dilated than two months previously.

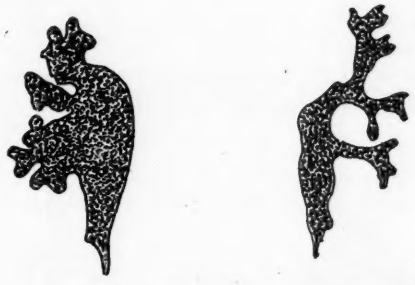

FIG. 396.—Six months after transplantation. Note that the right kidney, which previous to operation was normal, is now hydronephrotic, whereas the left kidney, which was hydronephrotic before operation, has now approached the normal.

November 9, 1936: 47 oz. of urine, which is much less offensive, have been passed in the last twenty-four hours. No abdominal distension, but slight tenderness in right loin. No fever. Tongue moist and clean. Mandelic acid prescribed.

November 16, 1936: Wound well healed. Loin tenderness has subsided. Patient is sitting up.

November 23, 1936: Urine is being passed twice at night and every 3 to 5 hours during the day. Patient is continent.

Excretion pyelography (*Fig.* 394): Dye is excreted at normal rate; good renal function. Both kidneys hydronephrotic.

November 27, 1936: Patient discharged from hospital.

January 25, 1937: Excretion pyelography (*Fig.* 395).

May 5, 1937: Patient re-admitted to hospital for examination pyelography (*Fig.* 396); left renal pelvis, calices, and ureter are still considerably dilated. The right renal pelvis is moderately well defined. General condition much improved. The following day total cystectomy performed.

Pathology of bladder growth: Base entirely involved by extensive, fungating growth. Microscopic section shows growth to be a papillary transitional-cell carcinoma.

November, 1937: Re-admitted with secondary growths in both inguinal areas. Patient died seventeen days later, with marked abdominal distension. Even within a few hours of death patient was able to hold urine for periods of four hours.

Comment.—The result in this case of ureteric transplantation was successful, and there is little doubt, in view of the low malignancy of growths of the bladder, that the patient would have been alive now were it not for the disease having been so extensive when cystectomy was performed.

E. L., female, aged 62 years. *Past history*: In 1917 patient commenced incontinence. She was seen by the late Mr. Frank Kidd, who performed an operation upon the urethra. In 1927 a further operation was performed by another well-known urologist, since when her incontinence, previously partial, has been complete. *Present history*: Complete incontinence of urine, necessitating changing garments three times daily. Unable to visit cinemas on account of her disability.

Examination shows scarring and stenosis in vagina, due probably to the two previous operations. Cystoscopy shows a normal bladder.

FIG. 397.—E. L., female, aged 62. Excretion pyelogram before operation. Pelves and calices well defined and normal.

FIG. 398.—Same case, six weeks after ureteric transplantation into bowel. Both kidneys functioning well, but calices and pelves dilated as compared with pre-operative condition.

FIG. 399.—Three months after transplantation. The pelves and calices of both kidneys are less dilated than they were previously.

FIG. 400.—Eleven months after operation. The pelves and calices show little change from those observed three months after operation.

Patient examined by Dr. Blake Pritchard, the neurologist, who diagnosed a complex neurosyphilitic disturbance, mainly of the tabetic variety. Normal Wassermann reaction of the blood.

February 3, 1938: Excretion pyelography (*Fig.* 397): Pelvis and calices well defined and normal.

February 10, 1938: Operation: Transplantation of both ureters into pelvic colon by usual technique. No dilatation of the ureters.

February 13, 1938: Urine has been draining well from the rectum, but as patient resented the presence of the rectal tube it has been removed.

February 14, 1938: Some abdominal distension, pain, and tenderness in the left loin. Temperature 99·8°.

February 21, 1938: General condition very good. Complete control of rectal micturition—2-hourly day and night.

February 28, 1938: Rectal micturition 4-hourly.

March 10, 1938; Sleeps undisturbed all night. No fever after the fourth day.

March 23, 1938: Excretion pyelography (*Fig.* 398): Kidneys functioning well and no marked hydronephrosis.

May 19, 1938: Excretion pyelography (*Fig.* 399).

January 13, 1939: Excretion pyelography (*Fig.* 400).

Comment.—Patient remains well and has complete control of the rectal micturition.

G. M., female, aged 45 years. History of pain in right loin radiating to pubis, occasional vomiting, and frequency of micturition, amounting at times to complete incontinence.

June, 1937: Cystoscopy: A very small bladder holding less than one ounce of fluid; deposit of phosphates on bladder base. Ureteric orifices not seen, even with indigo-carmine injection.

Excretion pyelography: Good excretion right kidney, pelvis and calices somewhat dilated; no X-ray evidence of excretion from left side.

Urine analysis: No tubercle bacilli found. *Bacillus proteus* grown in culture.

July 28, 1938: Operation for transplantation of right ureter, which was dilated, by the usual technique. The left ureter was found to be atrophied and therefore was not transplanted into bowel. Patient passed 6 oz. of urine by the rectum during the night following the operation. In the next twenty-fours she passed 26 oz., and on the fourth day she passed 76 oz. Patient complained of irritation from the rectal tube, so it was removed on the fifth day.

A week after operation patient could differentiate the passage of urine and fæces from the rectum. Less than a fortnight later patient had complete control of rectal micturition and could differentiate the passage of flatus, fluid, and fæces. Rectal micturition, once nightly and 3-hourly by day.

There was some fever during the first week after operation, but from the seventh day pyrexia ceased.

August 17, 1938: Excretion pyelography: Some delay in excretion of the dye from the right kidney; pelvis and calices dilated, right ureter also dilated. No function left kidney.

Comment.—This is a case of a systolic bladder due to chronic sepsis. It is probable that the left kidney was atrophic at birth. This patient is a scrubber at the County Hall and is now able to carry out her duties without inconvenience.

A. L., female, aged 34 years. Admitted to hospital for complete incontinence of urine, with a history of having had a number of operations. Patient is now wearing an apparatus on account of continued dribbling of urine.

Cystoscopy reveals a normal bladder, no organic cause discovered to account for the incontinence.

June, 1938: Operation: Transplantation of both ureters into the pelvic colon by the usual technique. No dilatation of either ureter. The following day patient passed 6 oz. of urine per rectum and during the following twenty-four hours 42 oz. Ten days later rectal micturition was four times during the day and twice during the night and there was full control.

Convalescence was apyrexial after the fifth day.

Pyelography one month after operation shows mild degree of bilateral hydronephrosis.

Comment.—The last time this patient was heard of she was in good health. She has had a criminal record and was an unsatisfactory patient.

E. E., female, aged 59 years. Admitted to hospital in April, 1938, with complete procidentia. On examination the procidentia was found to be the size of a toy rubber balloon, and on its surface were four big ulcers, which biopsy proved to be squamous-celled carcinoma (*Figs.* 401, 402).

April 26, 1938: Excretion pyelography (*Fig.* 405) showed well-marked dilatation of the pelves, with early clubbing of the calices of both kidneys. The bladder, which was within the procidentia, was shown by X rays (*Fig.* 403) to be filled by calculi.

April 28, 1938: Severe hæmorrhages from the carcinomatous ulcers necessitated urgent operation.

April 29, 1938: Both ureters were transplanted into the pelvic colon by the usual technique. The left ureter was dilated, but the right was of normal size. In the first twenty-four hours after the operation no urine was passed by rectum, but the following day she drained 18 oz. Three days later 38 oz. were passed in twenty-four hours. Ten days after

operation there was complete control of micturition, but there was frequency of 5 to 6 times during the day and twice at night.

May 28, 1938: Size of procidentia greatly reduced.

Excretion pyelography (*Fig.* 406) shows that the pelves of both kidneys are still dilated.

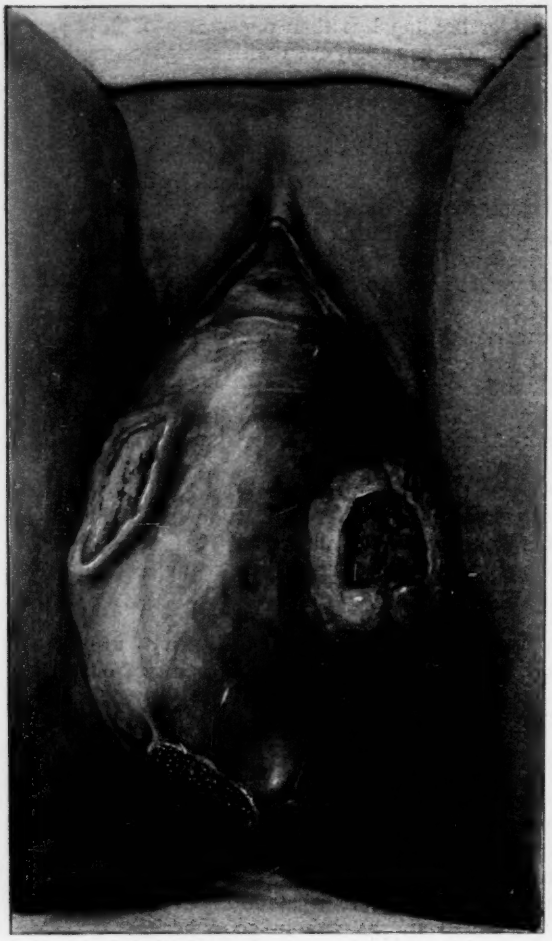

Fig. 401.

Fig. 402.

FIG. 401.—E. E., female, aged 59. Water-colour drawing of a complete procidentia. Note the three carcinomatous ulcers of the vaginal wall and the entrance to the cervical canal in the most dependent part of the tumour.

FIG. 402.—Same case. The complete procidentia held up by forceps. Note the multiple ulcers of the vaginal wall and a carcinoma close to the cervical canal.

June 9, 1938: Operation of excision of the procidentia was performed. The swelling consisted of the whole of the bladder, full of stones, the uterus and its adnexa, and the vagina. During the operation a slight tear was made in the rectum, and this was immediately closed with catgut sutures.

Three weeks later, the wound of the vulva having firmly healed (*Fig.* 404), an excretion pyelography was performed (*Fig.* 407). This showed less deformity of the renal pelves than in previous pyelograms.

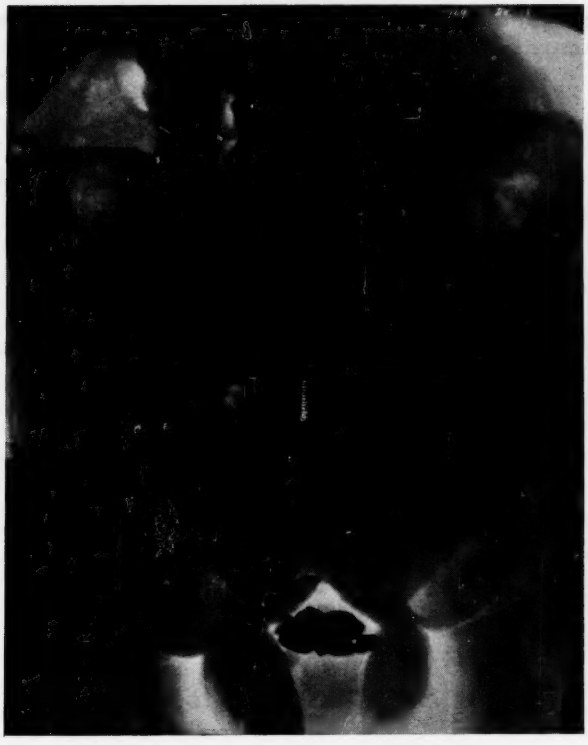

FIG. 403.—Same case. An X-ray picture of the pelvis, showing shadows of stones in the bladder. Note that the bladder is outside the pelvis.

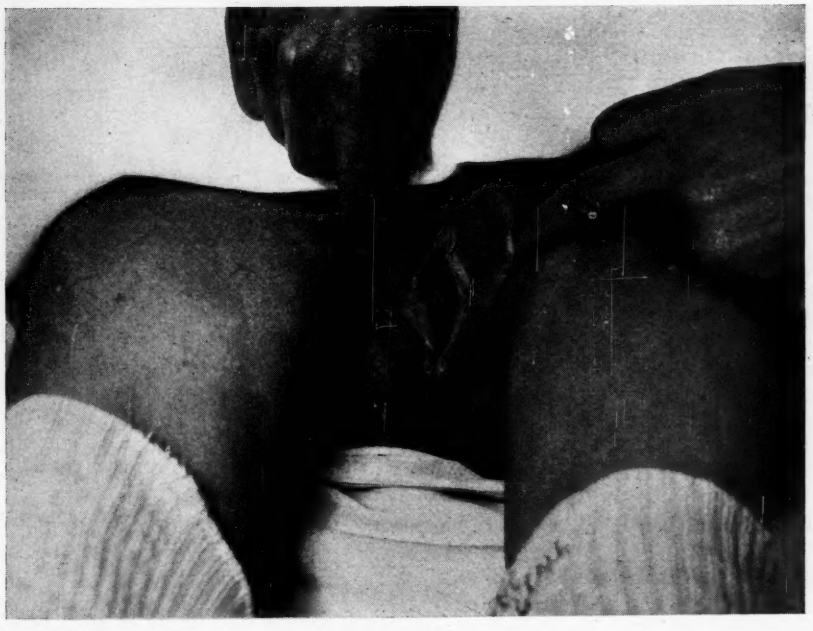

FIG. 404.—Photograph of the external genitalia one month after removal of the procidentia.

July 21, 1938: The patient was discharged from hospital in good health, with complete control of rectal micturition.

Three months later the patient returned to hospital with a prolapse of the rectum through the vulva. The scar of the buttonhole of the rectum, which occurred when the procidentia was removed, had given way. The patient was therefore re-admitted to hospital and the prolapse dealt with by freeing the margins of the bowel from the surrounding tissues and re-suturing the vulva.

The patient was discharged six weeks later in excellent health: rectal micturition normal and vulval scar firm and unyielding.

November, 1939: Patient was very well and had no nocturnal frequency. Pyelography showed a further reduction in the size of the renal pelves.

Comment.—This case may be considered a triumph for the operation of ureteric transplantation into the bowel. It is no exaggeration to say that by the surgical procedures which have been carried out her life has been saved.

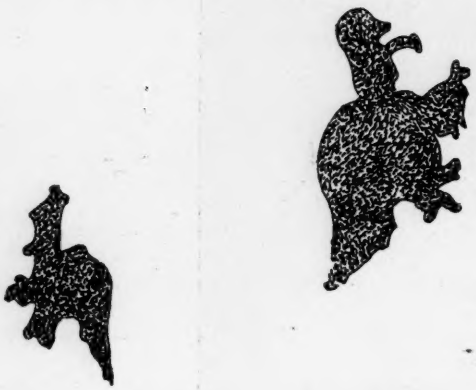

FIG. 405.—Same case. Excretion pyelogram before ureteric transplantation, showing hydronephrosis of both kidneys, but more advanced on left side.

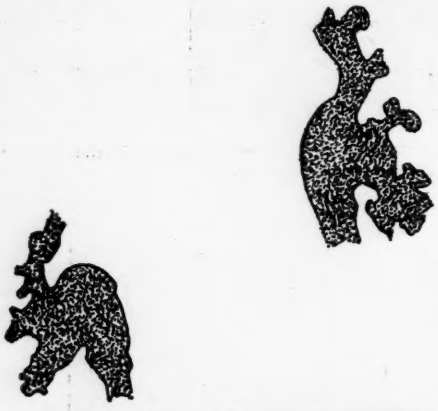

FIG. 406.—One month after transplantation, showing well-marked dilatation of both pelves.

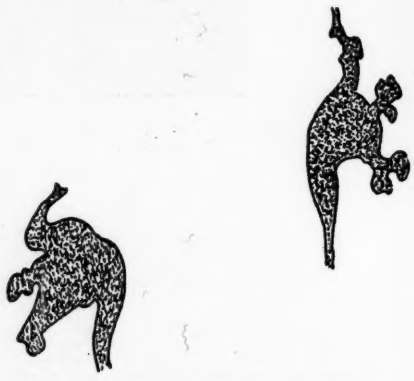

FIG. 407.—Seven weeks after, showing reduction in size of the pelves of both kidneys.

P. V. D., male, aged 54 years. Admitted to hospital in November, 1936, with a history of intermittent hæmaturia over a period of eighteen months.

In the same month a suprapubic cystotomy was performed for the removal of multiple sessile growths, which were surrounding the internal meatus and also involving the base of the bladder. The tumours were removed by endothermy current. The suprapubic wound healed slowly, and the patient was discharged from hospital in January, 1937.

In August, 1937, he had a recurrence of the bladder hæmorrhage. Recurrence of the growths had taken place round the internal meatus, which had almost completely blocked the urethra in this region.

The same month the operation of ureteric transplantation into the pelvic colon was carried out with the usual technique; both ureters were dilated.

Within a week of the operation the patient had complete control of the rectal micturition, but there was a two-hourly frequency by day and night.

In October, 1937, complete cystectomy was performed. The patient made an uninterrupted recovery from this operation.

An examination made in May, 1938, revealed the patient to be in good health, having complete control of rectal micturition, with a frequency of 4 hours by day and once by night.

The patient was examined again in June, 1939. There was no evidence of recurrence of the growth. He looked well, had put on a stone in weight, and there was no frequency of rectal micturition.

Comment.—The following letter from the patient demonstrates more clearly than any statement by his surgeons the value of the treatment which has been carried out on him: "In reply to your letter of the 31st ult., I shall be most happy to call and see you. Thanks to you I am feeling better now than I have felt for years."

C. F., female, aged 25 years. *Past history*: Since 14 years of age this patient had had frequency of micturition. Three years ago the frequency became more marked, being one or two hours by day and three or four times at night. Twelve months ago the frequency became half-hourly by day and night, and during the last four months she has been incontinent at night. She is wearing an apparatus. *Present condition*: Patient complains of pain in the right loin and right iliac fossa, nocturnal incontinence, and marked frequency during the day.

General examination: Patient is well nourished. She has a large mass in the right loin extending to right iliac fossa.

Cystoscopy attempted without anæsthetic failed owing to the inability to introduce any fluid into the bladder without causing great pain.

March, 1939: Cystoscopy under spinal anæsthesia. Bladder holds 3 oz., left ureteric orifice normal, the right ureteric orifice is drawn up and dilated, giving the appearance of a small diverticulum.

Excretion pyelography (*Fig.* 408) shows a normal left renal pelvis and calices; the right renal pelvis is just faintly outlined, and suggests gross pathological lesion on this side.

Radiograph of the chest shows some irregular fibrosis in the right upper zones consistent with lower-grade pulmonary tuberculosis.

Blood-urea, 45 mg. per cent. Urine: Tubercle bacillus not found in several specimens, but *Bacillus proteus* present.

March 16, 1939: Operation: laparotomy revealed a right ureter thickened to the size of the index finger; the left ureter was of normal size and was transplanted into the pelvic colon with the usual technique. A suprapubic drain was inserted, also a tube into the rectum.

FIG. 408.—C. F., female, aged 25. Excretion pyelogram before ureteric transplantation, showing no excretion of dye from right kidney. Left pyelogram normal.

FIG. 409.—Same case, one month after ureteric transplantation, showing very slight alteration from the normal of left kidney, no excretion from right kidney.

During the twenty-four hours after the operation the patient had drained by the rectum 13 oz. or urine, and in the next twenty-four hours she drained 42 oz. The patient had a slight shivering attack on this day, but there was no tenderness in the loin. This constitutional disturbance may have been due to redness and induration at the site of the intravenous injection of sodium sulphate owing to the escape of some of the fluid into the subcutaneous tissues.

Four days after operation rectal micturition was satisfactory; the bladder was catheterized and 2 oz. of pus and a little urine were drawn off.

March 21, 1939: Rectal tube uncomfortable and therefore removed. Has control of rectal micturition, but incontinent when attempting to pass flatus.

Six days later patient could differentiate between fluid, flatus, and fæces; rectal micturition 4-hourly by day and twice at night, with complete control.

April 13, 1939: Excretion pyelogram (*Fig.* 409): Left renal pelvis and calices clear and well defined, and only slightly more dilated than in pyelogram taken before the operation; no excretion from right kidney.

Patient discharged from hospital.

June 14, 1939: Patient was looking very well. She had full control of micturition; no nocturnal frequency. Still had pain in right kidney, which by palpation appears markedly enlarged. The bladder empties about 1 oz. of thick urine with each rectal evacuation.

July 20, 1939: Right kidney removed for a large tuberculous pyonephrosis.

November, 1939: She was in good health and had no nocturnal frequency.

Comment.—The patient's general state of health improved remarkably after the left ureter was transplanted into the bowel. She no longer had sleepless nights. Since the removal at a later date of the right kidney her health has remained good.

F. M. L. D., female, aged 59 years. Admitted to hospital with a six months' history of frequency of micturition and hæmaturia.

Cystoscopy showed a large extensive fungating carcinoma involving the right side of the bladder and the trigone.

April, 1939: An excretion pyelography shows slight hydronephrosis of the right side.

May 11, 1939: Operation: Transplantation of both ureters into the pelvic colon by the usual technique. No urine was passed per rectum during the first twenty-four hours, but on the second day 20 oz. were excreted. Four days after operation the rectal tube was removed on account of its failure to function satisfactorily; most of the urine was being excreted outside the tube.

May 16, 1939: The patient had a rigor, but there was no tenderness in the loins or complaint of pain. Rectal micturition frequency was half-hourly, but there was no incontinence.

May 22, 1939: Rectal micturition 4-hourly by day and twice by night. The abdominal wound was firmly healed.

Excretion pyelography, carried out on May 24, showed bilateral hydronephrosis, particularly on the left side.

May 29, 1939: She was discharged from hospital feeling well and able to discriminate between flatus, fluids, and fæces.

August 23, 1939: A total cystectomy was successfully performed.

November, 1939: She was examined and found to be quite well. There was no nocturnal frequency and no clinical evidence of the presence of malignant disease.

Comment.—Operation on this case is of such recent date that an expression of opinion as to the result of the treatment is inadvisable.

We have to thank the Principal Medical Officer for the London County Council for permission to publish this paper.

Our thanks are also due to Helen B. Graham for assistance in the reproduction of the pyelograms.

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THE POST-OPERATIVE RESULTS OF NEPHRECTOMY

By HOWARD G. HANLEY

In the early days of medicine it must have aroused much discussion as to why Nature should provide us with certain organs or viscera in duplicate. Curiosity must also have been felt as to whether both these organs were essential to life, or whether they were merely present as one of Nature's safeguards against disease or trauma. Information on the first point could only be gained slowly by observation, but, with the development of medical science, the experimental animal supplied the means of establishing the facts more definitely, and it was found in most cases that an animal could live without at least one of its paired organs.

Later came the problem of whether the loss interfered with the normal body functions, but this point was not so easily and dramatically explained as the previous one, and the question has been much debated.

With the advance of surgical technique, we have tended to assume that, if necessity arises we can do perfectly well without one of most of our bilateral organs. This assumption has been fairly established in regard to the kidneys since the first deliberate nephrectomy in a human being by Gustav Simon in 1869.

Various workers have since supported or refuted this assumption, while the experimental work performed on the sequelæ of nephrectomy in animals is very extensive.[1, 4, 6, 12] But experimental nephrectomy in an animal is not comparable with the same operation in a human being for various reasons. In the first place the animal is presumably perfectly healthy, while our patient in many cases is toxic or in a lowered state of health, due to the pathology of the kidney to be removed.

Secondly, in animal experiments the 'control' kidney can be presumed to be normal in the majority of cases, but in human beings requiring a nephrectomy we should not assume that the remaining organ is perfectly healthy. Indeed, in the case of a pyonephrosis, a tuberculous infection, or a stone-forming kidney, we may sincerely hope, but we should not really expect, such disease to be unilateral, particularly by the time surgical interference is called for. A continuance of the original pathological process can frequently be demonstrated in the remaining kidney long after a nephrectomy.

Our knowledge of the reserve capacity and of the compensatory hypertrophy produced by the removal of one kidney is practically limited to work done on animals, and it would seem therefore that any information obtained from observations on human patients would be of real value to surgery.

In an endeavour to add to our meagre knowledge on this subject, the present investigation was undertaken.

SOURCES OF MATERIAL

To avoid a comparison of results between individual surgeons and hospitals, all the case records of nephrectomies performed over a period of five years were followed up in two general hospitals and in one special genito-urinary hospital.

All these patients were written to, and they were asked, if possible, to attend the hospital at their own convenience for a thorough examination.

There were 213 case histories altogether, and of the 182 patients traced, 100 were actually examined clinically, and their renal function estimated. All the examinations and chemical estimations were performed by myself, so that any error was a constant one.

One difficulty in carrying out such an investigation lay in the selection of methods of estimating the renal function. The patients could only be examined as day cases in most instances, consequently the choice of tests was somewhat limited. It was eventually decided to perform a blood-urea and non-protein-nitrogen estimation on each patient, since these are more or less universal routine tests. The reliability of MacLean's urea-concentration test[9] appeared rather doubtful, so it was decided to adopt the Van Slyke urea-clearance test[10, 11, 13] in all cases, and to compare it with the urea-concentration test where possible. The advantage of Van Slyke's test is that it provides us with results as a percentage of normal, which can be used for comparison.

In most instances the urine was examined for pus cells and organisms; the urines of 16 tuberculous patients still suffering from marked frequency, etc., were injected into guinea-pigs, while the general condition of all the patients, including the blood-pressure, was recorded.

MODE OF PRESENTATION OF RESULTS

The 213 patients reviewed have been divided into six groups according to the original diagnosis—viz., hydronephrosis; pyonephrosis; calculus; tuberculosis; neoplasms; and an unexpected group, chronic nephritis.

The *operative mortality*, i.e., patients dying within a month of operation, has been calculated from the total of 213 operations performed.

The *total mortality*, which includes the operative and known subsequent deaths during the following five years at least, will be a minimum figure, since some of the untraced cases may also be dead.

The sex incidence in each pathological sub-group is about equal, except in the case of the neoplasms; here the disparity is sufficiently marked to be worthy of note even in so small a series—but of 27 patients there were only 4 women. The youngest patient in this review was 6·5 years, while the oldest was 69; the average ages at the time of nephrectomy in each group was as follows :—

	Years
Hydronephrosis	36·0
Pyonephrosis	39·1
Calculus	40·6
Tuberculosis	32·1
Neoplasms	55·1
Chronic nephritis	39·1

Hydronephrosis.—This group consists of 40 cases of nephrectomy for simple hydronephrosis without any evidence of infection, performed from two to six years previously. Of these 29 have been traced and followed up.

The *operative mortality* of the group was 5·0 per cent, with 2 deaths within a fortnight of operation.

The *total mortality* was 10 per cent, there being 2 further deaths within two years of operation, both dying in uræmic coma. No more deaths have occurred in this group during the last four years.

Examination of 18 patients showed them to be in good general health, but while the blood-urea was only markedly raised in one instance, 9, or 50 per cent of them, had a urea-clearance below 70 per cent, which, even on a generous basis, is below normal. No patient had a urea-clearance below 50 per cent, i.e., indicating definite renal failure, while none of the urines showed any gross infection. This is the only group without some residual urinary infection, and the only group without at least one clearance value below 50 per cent.

The most constant complaint of the patients in this group was an intermittent, dull ache in the region of the remaining kidney. Intravenous pyelograms demonstrated enlargement of the kidney or some degree of pelvic dilatation in 9 out of 12 cases X-rayed, as compared with the pre-operative plates.

Pyonephrosis.—This group consists of 44 operations for pyonephrosis during the previous two to six years. Only 4 cases are untraced.

The *operative mortality* was 20·2 per cent, 9 patients dying within a month of operation, 1 from a pulmonary embolism.

The *total mortality* was 34 per cent, there being 6 more deaths in the next two years. One of these followed a nephrolithotomy two years after the nephrectomy. No more deaths have occurred in this group in the last four years.

The *examination* of 24 patients showed that 7 of them were suffering from pyuria, with some cystitis and frequency.

The renal function was not so good as in the hydronephrosis group; 37·5 per cent of them were below 70 per cent of normal urea clearance, while 3 patients were showing signs of obvious renal failure, with a clearance below 50 per cent. One of these (*Case* 121) died subsequently (included in total mortality).

Lumbar pain was volunteered in several instances in this group, and radiographs of the remaining kidney showed enlargement, or early pelvic dilatation, in 5 out of 10 cases investigated.

Calculous Pyonephrosis.—This group consists of 49 cases of nephrectomy for calculus performed during the previous two to seven years. Of these 40 have been followed up.

The *operative mortality* was 6·1 per cent, with 3 deaths.

The *total mortality* was 16·3 per cent, with 5 further deaths, all of which were within two years of nephrectomy, except one boy who died five years later from a non-renal condition.

The *examination* of 27 patients showed that 1 had developed calculi in the remaining kidney. The renal function in this group must be considered definitely below normal; 55·5 per cent had a clearance below 70 per cent, while 5 other patients were obviously in poor health, with albumin or pus in the urine, frequency, etc., and a clearance value below 50 per cent.

Tuberculosis.—This group contains 48 nephrectomies for supposedly unilateral tuberculosis of the kidney, performed during the previous two to eight years. Of these 42 have been followed up.

The *operative mortality* was 4·1 per cent, with 2 deaths.

The *total mortality* by the end of six years had risen to 22·9 per cent (9 further deaths—6 within two years). One of these deaths occurred within three months of

operation, due to a breaking-down wound and a duodenal fistula; one in two years, immediately following a ureter transplant to the rectum for intractable cystitis; and another from phthisis.

Previous tuberculous history: Four patients underwent an orchidectomy six to ten years before the loss of the kidney; of these, 2 died as a result of the nephrectomy. One man survived a nephrectomy eleven years after a psoas abscess.

The *present condition* of the 31 known living patients was really far from satisfactory. Severe frequency, and in some cases dysuria, was a common complaint, even as long as eight years after operation. Sixteen persons, or just a third of the original number operated upon, considered themselves "cured", although their cystitis, etc., had taken three or four years to clear up in some cases. Four cases showed evidence of non-renal tuberculosis after the loss of a kidney. Three men had subsequent orchidectomy successfully performed, while one girl had an artificial pneumothorax induced four years after her nephrectomy. This patient is now married and well eleven years later.

The *examination* of 22 of the patients showed that 7 of them still had tubercle bacilli in their urine, i.e., 30·8 per cent, while another 4 still had a severe cystitis (*B. coli*) five years after operation.

The renal function of this group is comparable with the calculus cases in that over half (54·5 per cent) had a clearance value below 70 per cent, but only 2 cases (9 per cent) were below the 50 per cent mark. In view of the high post-operative morbidity of the group, one might expect the renal function to be even lower than it is, but most of the symptoms complained of were due to vesical causes; the only 2 patients with a clearance below 50 per cent had severe *B. coli* infections, with no trace of acid-fast bacilli on guinea-pig inoculation.

On reading through the case sheets, one could not help noticing the much greater pre-operative care and investigation which was taken over the tuberculous cases, as compared with all the other groups. It seems a pity that a survey of this sort gives one the impression that the only condition calling for a really exhaustive examination of the other kidney is tuberculosis. Everyone will agree that this is not so.

Neoplasms.—This group consists of 27 nephrectomies for new growths, as follows: Adenocarcinoma (Grawitz), 22; Malignant papilloma of pelvis, 2; Simple papilloma of pelvis, 2; Secondary carcinomatous deposit (primary unknown), 1. Only 1 patient could not be traced.

The *operative mortality* was 22·2 per cent—6 patients dying within a week of operation.

The *total mortality* within the next two years rose to 63 per cent, 9 dying within thirteen months, and another 2 within the two years. Six of these patients were known to have died with extensive secondary metastases; in 2 the cause of death could not be ascertained, but the remaining 3 died in uræmic coma.

The *examination* revealed 8 patients alive 2, 3, 6, 7, 8, 8, 10, and 11 years after operation. Of these 6 originally had a Grawitz tumour, 1 a carcinoma of the pelvis, and 1 a simple papilloma of the pelvis. The general health of this group appeared to be perfectly normal, except for one man with a severe *B. coli* cystitis, and one man complaining of pain in his shoulder. This was found to be a secondary deposit in his scapula. The patient soon died, and is included in the total mortality above.

The *renal function* of the 8 survivors as a group was better than that of any of the other groups. Only 1 patient had a urea clearance below 70 per cent, while only the man with the metastases in his scapula was below 50 per cent.

A neoplasm would appear to be the only genuinely unilateral condition affecting the kidney, and it is interesting therefore to observe that those who survived two years had a renal function adequate for their needs, did not develop any further metastases, and were in good health at the time of writing, at least five years after operation.

Chronic Nephritis.—This group consists of 5 patients whose kidneys after removal showed evidence of chronic nephritis, with no histological evidence of any other pathology. Three of them suffered from unilateral hæmaturia over varying periods of time, and a diagnosis of tuberculosis was made. The remaining 2 cases had painful, ptosed kidneys—one unrelieved by a previous nephropexy.

The *operative mortality* was 20 per cent, with 1 death eight days after operation.

The *total mortality* was 100 per cent, all of the cases dying within eight months of nephrectomy. Since chronic nephritis is a progressive and bilateral condition, it is only to be expected that the mortality should be so high. In none of these cases was there anything to indicate the true nature of the pathology before operation.

THE RENAL FUNCTION TESTS USED

Blood-urea and Non-protein Nitrogen.—All the blood-urea and non-protein-nitrogen estimations recorded in this paper were performed in duplicate to minimize any error. Of the 100 patients examined, only 12 showed a blood-urea of over 40 mg. per cent, and each of these 12 had a urea-clearance value of under 65 per cent of normal.

In only 10 out of 68 patients was the non-protein nitrogen raised above 40 mg. per cent; in only 5 was it over 50 mg. per cent. While demonstrating the enormous renal reserve we possess, this also demonstrates the comparative grossness of the two tests, which cannot even detect a loss of 50 per cent of our renal tissue.

Van Slyke Urea-clearance Test.—The data required by the laboratory staff in calculating the results of this test are: (1) The blood-urea; (2) The volume of urine in c.c. excreted per minute; and (3) The percentage of urea in the urine specimens collected.

The collection of blood and the chemical estimations are simple matters. Moderate errors in the chemical analyses do not make much difference to the clearance figure, but even very small errors in the factor V (i.e., c.c. per minute) influence the final result. For this reason the accurate collection, measurement, and timing of the urine specimens is all-important, and should be in the hands of a skilled, interested laboratory technician at least, if the test is to be of any value.

I personally measured, timed, and collected all the specimens recorded in this paper, a fact which made it possible to impress upon the patient the importance of completely emptying the bladder, and when in doubt, of trying again.

This, like any other renal function test, is far from infallible, having a probable variation in standard clearance of $\pm$ 10 per cent; therefore the results must not be taken as of mathematical exactness, but this investigation shows that the test is sensitive enough to detect a loss of 50 per cent of our renal tissue in most cases, since the average clearance figure was 73 per cent or just below normal.

MacLean's Urea-concentration Test.—With the object of estimating the value of this test, which is almost universally popular, a small series of the patients were examined by the urea-clearance and the urea-concentration tests on consecutive days, and the results are given in *Table I.* It will be seen that in only one instance, *Case* 24, with a clearance value as low as 48 per cent, was the concentration figure below 2 per cent. Three patients, *Cases* 6, 7, and 30, were under 2·5 per cent, *Cases* 7 and 30 having a clearance value of under 55 per cent.

Here again, a loss of half the renal tissue is undetected by the test.

Table I.—A COMPARISON OF THE VAN SLYKE UREA-CLEARANCE TEST AND THE MACLEAN UREA-CONCENTRATION TEST

CASE NO.	CAUSE OF NEPHRECTOMY	NON-PROTEIN NITROGEN	BLOOD UREA	VAN SLYKE	MACLEAN UREA-CONCENTRATION TEST			
					Before urea	1st hour	2nd hour	3rd hour
		mg. per cent	mg. per cent	per cent	per cent	per cent	per cent	per cent
6	Pyonephrosis	35	27	73	1·55	1·42	2·26	0·25
7	,,	33	21	54	1·72	1·90	2·26	1·90
10	,,	30	22	70	1·69	2·54	2·66	2·54
13	,,	20	15	105	1·55	2·26	3·00	—
17	,,	26	22	70	1·55	2·54	2·26	2·54
22	,,	30	22	86	1·0	1·58	2·26	2·82
24	,,	40	33	48	0·48	1·14	1·98	1·98
30	Hydronephrosis	33	23	55	1·0	1·42	1·55	2·26
36	,,	43	35	67	1·41	2·68	1·98	—
61	,,	31	21	74	0·48	2·54	1·98	1·72
62	,,	33	26	40	2·26	2·82	2·94	2·38
63	,,	30	18	98	1·41	1·97	2·82	1·58
85	Tuberculosis	20	17	120	2·40	2·68	2·54	2·82

DISCUSSION OF RESULTS AND CLINICAL FINDINGS

Briefly summarizing the *renal function results*, we find that the blood-urea and non-protein nitrogen are practically within normal limits, giving no indication that there has been any gross loss of renal tissue, whereas the average urea-clearance of the 100 patients was just below normal. Fifty of them had a clearance figure below 70 per cent, and among these were to be found the majority of the 38 patients with definite symptoms.

Eleven patients had a reading below 50 per cent; all of these could be described as 'ill', and four of them have since died.

Turning now to the *general examination* of the 100 patients investigated, it was found that 38 of them still had various symptoms sufficient to cause inconvenience, chiefly in the nature of dysuria and frequency, while many of them had infected urines. This was chiefly seen in the pyonephrotic, calculous, and tuberculous groups. No case of incisional hernia was seen, but there were two discharging sinuses and one fæcal fistula.

On the other hand 62 patients, or less than a half of the survivors, felt perfectly fit, having no complaints of any sort apart from occasional aching pain in the region of the remaining kidney. The blood-pressure was only raised in one man; he was re-admitted and died of chronic nephritis.

A fact worthy of putting on record is that 6 women became pregnant from two to four years after their nephrectomy. Five of them had perfectly normal deliveries without any renal trouble as far as I can ascertain from their doctors, while the sixth patient had two miscarriages within a year of operation, and was then lost sight of.

The only comparable investigation I can find in the literature is the work of Ellis and Weiss in 1933,[3] who published their examination of 12 patients who had undergone nephrectomy from a few days to six years previously. The results of these workers are interesting, for they have investigated their cases in a somewhat similar way to my own series, using the Van Slyke clearance test. Nine of the 12 patients were in good health clinically, and of these 7 had a renal efficiency of over 75 per cent. The 3 remaining patients had complications in the nature of pus and albumin in the urine, showing implication of the remaining kidney with the original disease of pyonephrosis, while the renal efficiency values were only 29 per cent, 35 per cent, and 47 per cent respectively.

Analysing these cases in the same way as my own, 5 of the 12, or 41·6 per cent, have an average renal efficiency below normal as compared with my figure of 56 per cent. The average efficiency of the whole twelve patients comes to 82 per cent, whereas in my series it comes to only 72·8 per cent. None of these authors' cases showed an abnormally high blood-urea, while only one had a raised blood-pressure, and this was present before nephrectomy.

These American workers conclude that when a patient is examined immediately after nephrectomy the renal function is definitely lowered, both as to concentration and clearance tests, but that as compensatory changes occur the efficiency improves. The present investigation confirms this finding. But they then continue: "In the absence of complications, the renal function of patients with only one kidney is not only adequate, but possesses a reserve capacity as well". This is contrary to the findings in the present investigations, and it is probable that the results of Ellis and Weiss are due to their being fortunate enough to encounter 5 cases in their 12 with a renal efficiency over 100 per cent. There were only 13 patients with a figure over 100 per cent in this present far larger series of cases. Also, their tests were performed on subjects lying in bed, and in a fasting state.

The phrase used by these two workers, "in the absence of complications", is undoubtedly the crux of the matter, and it seems that these complications, such as a continuation or extension of the original pathology in the remaining kidney, are present in far more cases than surgeons generally realize. The fact that 8 out of the 11 'ill' patients with a clearance below 50 per cent were to be found in the pyonephrosis and calculous pyonephrosis groups, supports this assumption, and would strengthen the belief that infection reduces the renal efficiency more than any other single factor.

The lumbar ache on the sound side, referred to above, was complained of by so many otherwise perfectly fit patients that an attempt was made to ascertain radiologically whether any changes in the nature of compensatory hypertrophy could be responsible.

Compensatory Renal Hypertrophy.—A considerable amount of research by different workers has been performed on the degree of compensatory hypertrophy after nephrectomy, using experimental animals.

The conclusions arrived at appear to be much the same in most cases, and are, briefly stated, that the remaining kidney does definitely undergo a compensatory

Table II.—RADIOLOGICAL INVESTIGATION OF THE REMAINING KIDNEY

CASE NO.	SIDE OF NEPHRECTOMY	SEX	AGE AT TIME OF OPERATION	MONTHS SINCE NEPHRECTOMY	UREA CLEARANCE	CAUSE OF NEPHRECTOMY	PRESENT SYMPTOMS	X-RAY REPORT
					per cent			
1	R	F	34	90	63	Pyonephrosis	Well	S, No change in size of kidney
7	L	F	15	54	70	,,	Swelling of ankles, headache, abdominal pain, albumin in urine. B.P. 135/85	S, Enlarged right kidney
11	L	F	28	48	70	,,	Well, but occasional pain right side	P, Enlargement and early pelvic hydronephrosis on right side
16	L	M	59	30	64	,,	Occasional pain on opposite side	S, No appreciable change in size of right kidney
18	R	F	29	27	54	,,	Well	S, No change in size of left kidney
23	R	F	37	12	105	,,	Well	P, Normal pyelogram
24	L	F	16	12	73	,,	Swelling of ankles. Albumin in urine. B.P. 130/90	P, Enlargement of right kidney but no hydronephrosis
25	R	M	31	6	48	,,	Pain on left side, frequency, nocturia, pyrexia, pus in urine	P, Enlargement of left kidney with poor function = pyonephrosis
26	L	M	46	3	64	,,	Well	S, No appreciable change in size
27	L	F	36	9	74	,,	Cystitis, pain in opposite side and back, pus in urine	P, No increase in size of kidney but early hydronephrosis
31	R	M	20	36	92	Hydronephrosis	Pain on opposite side	S, No enlargement of left kidney
32	L	M	51	30	102	,,	Well. B.P. 150/100	P, Enlarged left kidney and early pelvic hydronephrosis
38	L	M	43	15	110	,,	Well	P, Enlargement of right kidney and early pelvic hydronephrosis
39	R	F	14	12	55	,,	Occasional pain on left side	P, Early pelvic hydronephrosis
41	L	M	43	6	90	,,	Sinus still open	P, Enlarged kidney shadow
42	R	F	33	6	68	,,	Occasional pain on left side	P, Enlargement of right kidney

39	R	F	14	12	55	,,	Occasional pain on left side	P, Early pelvic hydronephrosis
41	L	M	43	6	90	,,	Sinus still open	P, Enlarged kidney shadow
42	R	F	33	6	68	,,	Occasional pain on left side	P, Enlargement of right kidney and early pelvic hydronephrosis
43	L	F	26	3	62	,,	Well	S, Enlargement of right kidney
132	L	F	43	21	47	,,	Well, but severe right-sided pain	P, Enlarged kidney, pyelectasis and early clubbing of calices
134	L	M	36	14	52	,,	Pain right side, within 10 months of operation; 2 years later, appendicectomy. No relief. Now albumin and ankles +	P, Slight dilatation of right pelvis
135	L	F	23	23	63	,,	Pain right side, otherwise well	P, Pyelectasis right side
54	R	M	55	15	100	Hypernephroma	Well	S, Enlarged left kidney
63	L	F	15	54	86	Calculi ,,	Pain on opposite side, swelling of ankles, no albumin in urine P	? Early pelvic hydronephrosis right side
71	R	M	26	15	61	,,	Nephrostomy on left kidney 6 months after right nephrectomy	No appreciable enlargement of left kidney
75	R	F	59	3	80	,,	Well	P, No change in pyelogram
87	R	F	21	44	120	Tuberculosis	Frequency + +, nocturia, but feels well otherwise	P, No change
88	R	M	29	42	85	,,	Well	S, No change in size of left kidney
90	R	F	23	30	39	,,	Scanty and irregular menses, only fair general health	S, Enlargement of left kidney
91	L	M	11	21	65	,,	Incontinent, enuresis, albumin and pus in urine	P, Enlargement and hydronephrosis of right kidney
92	L	F	36	21	98	,,	Well	S, No appreciable change
94	L	M	23	15	100	,,	Feels well, putting on weight	P, No change in size or hydronephrosis

S, Straight radiograph; P, Intravenous pyelogram.

hypertrophy in some cases due to its extra work.[4, 6, 13] According to Aratki,[2] this hypertrophy is shown by an increase in size and weight and by glomerular enlargement, while MacCullum[7] believes there is also tubular enlargement, and that this is made possible by an actual increase in the number of living cells. Moore,[12] while confirming the glomerular enlargement, has established the fact that there is no increase in their number.

Most workers seem to find that this compensatory hypertrophy only occurs in young animals. On this point MacKay, MacKay, and Addis[8] consider that hypertrophy is less as age advances, due to decrease in growth capacity. They found that in albino rats, hypertrophy took place within forty days of ablation of one kidney, and was then practically stationary.

I can find no record of any systematic investigation of the hypertrophy taking place in human beings after nephrectomy, although the presence of an enlarged remaining kidney is occasionally noted at autopsy on such a patient. With the object of obtaining more definite information on this subject, a selected number of the nephrectomized patients were re-X-rayed for increase in kidney shadow. Definite pelvic dilation or enlargement of renal outline could be demonstrated in 15 out of 31 cases where suitable pre-operative films were available for comparison. I consider that there is room for much valuable research into this question, and I regret that I have not so far had the opportunity of collecting a larger series of cases, but my observations on these few patients support the belief that hypertrophy does occur after nephrectomy, and that it is sufficiently gross to be detectable on an X-ray plate in many instances.

The very small number of cases available makes it impossible to form any opinion as to the frequency or degree of hypertrophy occurring, or to the relative liability of the right or left kidney to these changes. Neither is there any obvious factor responsible for producing these changes in some of the cases and not in others.

Hypertrophic changes took place in the pyonephrosis and hydronephrosis groups with much the same frequency; while the renal efficiency bears no relation to the radiological findings. Another interesting and important point is that the age of the patient when the nephrectomy is performed does not bear the same relation to the incidence or degree of hypertrophy which will follow as one might expect. Two of the cases showing the biggest increase in shadow were still under 20 years of age, but the others included a multiparous woman of 33 years at the time of operation, and two men of 51 and 53 years respectively.

It would appear from this that the power of hypertrophy in the human kidney still remains active in adult life, whatever it may do in the experimental animal.

A glance at *Table II*, column 5, shows the number of months between nephrectomy and the present investigation, and it will be seen that enlargement and early pelvic dilatation are detectable as early as three months after operation. Therefore if hypertrophy is going to be gross enough to be detectable radiologically in three months, it must start immediately after operation. The slow steady rise in renal efficiency during the early convalescent days may be connected with this phenomenon of hypertrophy, but I could demonstrate no relationship between the presence of enlargement and the ultimate renal function.

Ordinary increase in the size of the renal outline is easily understood, but why a pelvic type of dilatation should develop in a kidney after removal of its fellow is difficult to explain. No urinary obstruction could be demonstrated in any of these

cases, nor was there any dilatation of the ureter. They are just like Hosford's "idiopathic group of hydronephrosis".[5] The concentration of dye was good in every case, regardless of the renal function tests.

I am not including in this paper a review of the literature, or making any suggestions as to the causation of the pelvic dilatation, but, if it is part of a compensatory mechanism it is interesting to realize that after a nephrectomy the solitary kidney is made to excrete twice its usual volume of urine in the twenty-four hours. Ten patients investigated excreted 1500–2000 c.c. of urine per day for a week.

A study of the post-operative urine charts of all these nephrectomies demonstrates that it is about ten days before the 24-hour urine returns to normal in most cases.

With regard to the lumbar pain complained of by these nephrectomized patients, it is impossible to say definitely whether compensatory changes are responsible or not, since it was noted in patients showing no such X-ray changes. On the other hand, numerous patients inferred that the pain was more noticeable during a sudden spell of cold weather, or after drinking beer, two conditions leading to a polyuria and presumably to distension of the renal pelvis.

SUMMARY AND CONCLUSIONS

A general survey of the 213 patients reviewed is given in *Table III*. The first striking fact is the high operative mortality of 10·7 per cent. This figure is largely due to the 9 deaths in the pyonephrosis and 6 in the neoplasm group. It was noticeable that the poor general condition of the patients before operation was mentioned in several instances in the notes of these two groups.

Table III.—General Summary of Cases Studied

	Hydro-nephrosis	Pyo-nephrosis	Calculus	Tuber-culosis	Neo-plasms	Chronic Nephritis	Totals
Total number of cases	40	44	49	48	27	5	213
Number of cases untraced	11	4	9	6	1	0	31
Number of cases traced	29	40	40	42	26	5	182
Number of cases examined	18	24	27	22	8	1	100
Operative mortality	2 (5%)	9 (20·2%)	3 (6·1%)	2 (4·1%)	6 (22·2%)	1 (20%)	23 (10·7%)
Total mortality	4 (10%)	15 (34%)	8 (16·3%)	11 (22·9)	17 (63%)	5 (100%)	60 (28%)
Number known to be alive	25	26	31	31	8	0	121
Cases with renal efficiency between 50 per cent and 75 per cent	10 (55·5%)	10 (41·6%)	14 (51·8%)	13 (59%)	2 (25%)		49%
Cases with renal efficiency below 50 per cent	0	3 (12·5%)	5 (18·5%)	2 (9%)	1 (12·5%)		11%
Total number of cases under 75 per cent	10 (55·5%)	13 (54·1%)	19 (70·3%)	16 (68%)	3 (37·5%)		60%

Of the 182 patients traced, a further 37 died after leaving hospital, bringing the total mortality up to 28 per cent. Of the 37 late deaths, 34 occurred within two years of operation and were mostly from renal failure. Two other patients, both suffering from renal tuberculosis, lived four and five years respectively before being readmitted with suppression of urine to die in coma.

The remaining death was a boy who died four years after his operation, from the results of a wasp sting at camp. This would indicate that should the renal reserve after a nephrectomy be insufficient for the patient's needs, failure will show itself early—in this series within two years. Two men who were examined within eight months of operation, and who had a urea clearance of under 48 per cent, were both dead within a year.

The late deaths (3 and 5 years) in the tuberculous group can be explained by the fact that the renal lesion is merely a local manifestation of a generalized disease, which is not cured by a nephrectomy *per se*, consequently the remaining kidney or other organs are likely to become involved at any time.

In the neoplasm group 11 late deaths occurred in two years—6 from metastases. But even here, at least 4 persons are known to have died of renal failure with suppression and coma. On the other hand, the knowledge that 8 patients are alive and well, 6 of them five years later, is most encouraging.

The next highest delayed mortality occurred in the pyonephrosis and calculous pyonephrosis cases, where 11 deaths are recorded, again within two years of operation. Infection would seem to be one of the chief factors responsible for lowering the renal efficiency. This is supported by the finding of only 2 delayed deaths in the simple hydronephrosis group.

Before leaving this point, it is unfortunately impossible to avoid making a comparison of the figures derived from the different sources. A study of the case-histories demonstrates the extensive pre-operative investigation and preparation, and the conservative choice of cases considered fit for a nephrectomy, employed in the special genito-urinary hospital. These facts, coupled with three "accidents" in the general hospitals' figures, viz., a pulmonary embolism, a bronchopneumonia, and a 'slipped pedicle', largely account for the difference in the mortality figures as follows :—

Special hospital :	Operative mortality	4·8 per cent
	Total mortality	21·6 „
General hospitals :	Operative mortality	13·9 „
	Total mortality	29·3 „

The *chronic nephritis* cases are interesting: Repeated severe hæmorrhage, always from the same kidney, was the chief symptom in 4 instances, while more or less severe pain is mentioned in 5. The renal function before operation, as shown by the blood-urea and urea-concentration tests, was normal in all cases, while only 1 had albumin in the urine. No rise of blood-pressure was recorded. Two of these patients were re-admitted to hospital before death in a uræmic state, 1 dying of a cerebral hæmorrhage with a blood-pressure of 200/140.

It would be of value to know how many other kidneys have been removed and later found to be nephritic, since the prognosis is obviously bad with such a progressive and bilateral disease.

From the *clinical aspect* 38 per cent of the patients examined still had symptoms severe enough to cause inconvenience; 60 per cent of them had a renal function

below normal, while 11 were definitely 'ill' and exhibiting signs of renal failure. Four of these have since died. This only left 40 out of the 100 patients examined who could be considered satisfactory. Of the 122 known living patients, 62 (50.8 per cent) of them volunteered the information that they felt and considered themselves " perfectly well ".

Incidentally, no relation could be established between the sex or the age of the patients and the ultimate prognosis or renal efficiency to be expected after a nephrectomy, but it would appear that, contrary to general belief, the renal function following such an operation is not always sufficient for the patients' later needs, and undoubtedly a more accurate estimation of the efficiency of the remaining kidney, before removal of its fellow, would be invaluable.

That this information cannot be satisfactorily obtained by using blood-urea or urea-concentration estimations, is shown by the results in this paper. But the Van Slyke clearance test appears to be much more sensitive, and I should think that a value consistently below 60 per cent of normal should negative any radical surgery, whatever the blood-urea figure might be.

With regard to the *renal pain* developing on the sound side, radiological comparisons of the remaining kidney before and after removal of its fellow definitely prove the presence of compensatory hypertrophic changes in some cases, but not in all.

Although nephrectomy experiments show that hypertrophy is practically limited to young animals, such compensation is certainly not confined to young human subjects, the oldest example in this series being 53.

Not all the patients complaining of pain showed an enlarged kidney, while some cases had hypertrophic changes and no pain. Therefore it would be unwise in so small a series of observations to establish any definite relationship between the pain and the hypertrophy.

Of greater interest was the finding of a pelvic type of hydronephrosis in the remaining kidney in some instances. This was detected as early as three months after nephrectomy, and was frequently associated with the lumbar pain. Again the series is too small to prove any relationship between this dilatation and the renal pain, or between these two occurrences and the age, sex, or renal function.

No explanation is being put forward in this paper to explain the development of this pelvic type of hydronephrosis. No organic obstructive factor could be demonstrated, and there is obviously much room for further research into this subject, since I can find no reference to such phenomena in the literature.

In the present state of our knowledge nephrectomy is the only available treatment for many renal conditions, but in view of the findings in this investigation, where over a quarter of the patients are dead within two years, and only half of the survivors are completely relieved of their symptoms, there should be no complaisant easing off in the search for more conservative meaures, particularly in the hydronephrosis and calculous cases. A better selection of the time to operate, following the lines of prostatic surgery, would probably improve the results all round.

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EXPERIMENTAL SURGERY

HEPARIN IN THROMBOSIS AND EMBOLISM*

By GORDON D. W. MURRAY, Toronto

Heparin was discovered by Howell in 1916 and he showed that it increased the coagulation time of blood. No experimental work was done to prove whether it had any effect on thrombosis in blood-vessels. Thrombosis and obliteration of the lumen may result from injury of the intima of blood-vessels by various means, as Welch,[2] Zurhelle,[3] Schimmelbusch,[4] and Zahn[5] have shown. They have described the accumulation of platelets at the site of injury. Very soon leucocytes were added to the mass of platelets, and finally fibrin made its appearance, so that, ultimately, the ordinary blood-clotting processes were added to those of the earlier thrombus. As these changes have been fully described by these investigators, no attempt was made to repeat their work in our experiments.

As it was our object to study whether heparin would prevent these processes, different means of producing thrombi with moderate certainty were investigated. We found[6] that superficial veins in the extremities of dogs may be moderately severely traumatized without producing thrombosis, but finally we developed a technique by which thrombosis could be produced in well over 80 per cent.

CONSTITUTION AND ACTION OF HEPARIN

Chemistry.—Howell's[12] conclusion from his observations on his newly discovered substance, heparin, was that it was probably a glycuronic acid derivative or condensation product. In 1933 Schmitz and Fischer[13] succeeded in preparing a crystalline brucine salt which had thirty-two times the activity of the original material. In a subsequent paper[14] they stated that heparin is probably a carbohydrate compound with a molecular weight of about 650.

In 1933 Charles and Scott,[15] working under Best, published their methods of preparation and their analysis of heparin. They succeeded in isolating heparin in pure form from ox lung, as a barium salt. Taking advantage of the fact that benzidine forms an amorphous precipitate with heparin, they prepared this derivative. When freed of benzidine, a product with only 0·7 per cent ash was obtained. From this the crystalline barium salt was readily prepared, which yields 33·5 per cent ash and only 0·4 per cent amino nitrogen. The barium was removed, by several reprecipitations, with benzidine. This preparation gave the following analyses: calcium

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* A Hunterian lecture was given on the basis of this paper in the Royal College of Surgeons in June, 1939.

Apart from the references given the experimental work described in this paper was developed by the author and carried out during the past seven years in collaboration with Professor C. H. Best in the Department of Physiology, University of Toronto, and with Professor W. E. Gallie in the Department of Surgery, University of Toronto, in the Toronto General Hospital.

23·1 per cent; hydrogen 4·99 per cent; nitrogen 2·1 per cent; sulphur 11·54 per cent. The empirical formula assigned was $C_{25}H_{65}O_{50}N_2S_5$. The anticoagulant action was about 500 Howell units per milligram.

Recently Jorpes and Bergstrom[16] were able to show that the amino sugar in the purified form is glucosamine, which is a characteristic component of mucoitin, and consequently to classify heparin as a mucoitinpolysulphuric acid. Its close relationship to the more commonly known chondroitinsulphuric acid is established. The structure of a unit of mucoitin is shown in the accompanying formula by Jorpes and Bergstrom (*Fig.* 410). The points where sulphuric acid may be attached are designated by X. Three such radicals may be attached, making heparin, mucoitintrisulphuric acid. Heparin is the strongest organic acid known.

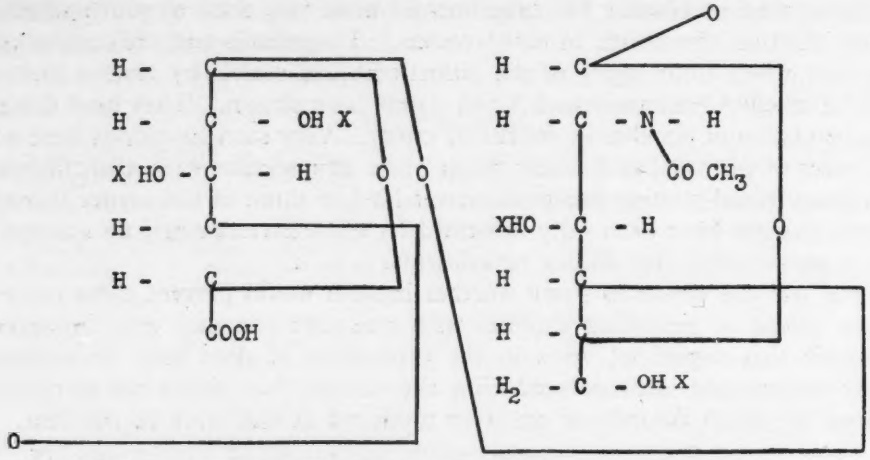

FIG. 410.—Suggested formula of heparin by Jorpes and Bergstrom. X shows where esterification with sulphuric acid may take place.

Source of Heparin.—Originally heparin was isolated from dog liver, by Howell.[7] Charles[8] and Scott found heparin widely distributed throughout many tissues and organs. Ox liver, muscle, and lung yielded comparable amounts, with the richest yield in lung. Much smaller quantities were obtained from heart, thymus, spleen, and blood.

Histological investigations by Jorpes[9] and his co-workers have shown a wide distribution of heparin in tissues. Lison[10] had shown that the metachromatic staining reaction with toluidine blue is due to the presence of mucoitin and chondroitinsulphuric acids. The colour, with heparin, is about one hundred times more intense, and this intensity of colour is like the reaction given by the granules of the mast cells of Ehrlich. The morphology, chemistry, and function of these cells is exhaustively discussed in a paper by Holmgren and Wilander.[11] With this method of investigation, the wide distribution of mast cells in the connective tissue surrounding blood-vessels, in the walls of blood-vessels themselves, and especially in the venæ cavæ, was shown. This might account for the delay in post-mortem clotting in these vessels. Large numbers of mast cells were found in the cornea, which might account for the absence of clotting when small hæmorrhages occur in this region.

The heparin provided by the Connaught Laboratories in Toronto is obtained from ox lung. The yield per hundred pounds is about one gramme of the purified

crystalline barium salt. This purified product has a potency of 100 units per milligram. The unit in this case is equal to about 5 units as originally described by Howell.

Heparin is available in 10-c.c. vials containing 1000 units per c.c. Two years ago the cost of one vial was twenty-five dollars (or five guineas), but with an increased yield and a greater demand, the price has been reduced to about five dollars (or one guinea).

We are waiting and hoping that some clever chemist will synthesize heparin or discover some equally effective non-toxic substance. Many efforts to accomplish this are being made, including those of Charles.

An interesting observation has been made by Waters[51] and Howell[22] that during anaphylactic and peptone shock the blood of the animal becomes incoaguable. It has been shown by Best and Jaques[52] that the anticoagulant in this blood is heparin, as purified heparin crystals have been formed from extracts from this blood.

Physiological Action.—It is not the object of this paper to discuss the virtues of the many theories of blood-clotting, but most authorities agree that in circulating blood there exist prothrombin, antiprothrombin, fibrinogen, and calcium ions. As heparin has been demonstrated in normal blood, it is probably the normal antiprothrombin, as described by Howell. In shed blood thromboplastic substance (cephalin), liberated from injured tissues or platelets, combines with antiprothrombin (heparin). The prothrombin then reacts with calcium ions forming thrombin, which permits conversion of fibrinogen to fibrin. By this theory heparin is an antiprothrombin.

According to Mellanby[17] heparin acts as an antithrombin, but Quick's[18] general conclusions from his work supported Howell's theory.

From all the evidence, heparin probably is the normal anticoagulant in circulating blood, and either assists or is necessary in maintaining blood in its fluid state. Its action may be largely to activate a precursor to antithrombin, rather than to combine with prothrombin or thrombin to make them insensitive to cephalin.

Chargaff and Olson[19] made the important observation that heparin and protamine combine in the proportion of 0·3 mg. of the former to 1 mg. of the latter and in this state the anticoagulant action of heparin disappears. Chargaff[20] also found that protamine and cephalin form an insoluble complex, which may explain the fallure of protamine to shorten the coagulation time of chicken plasma, i.e., to demonstrate the presence of small amounts of heparin in normal blood.

Another interesting effect of heparin which must ultimately be left to the physiologist to explain, is its influence on platelets. Through a glass cell in an artificial loop in the circulation between an artery and a vein, Best[21] obtained a pictorial record with a moving picture camera of the action of some of the cells in the circulating blood-stream. With a scratch on the inside of the glass, the platelets accumulated very quickly under ordinary conditions. Rapidly enlarging clumps of platelets extended downstream from that point. Under ordinary conditions these masses of platelets increased until, within about one hour or less, a tube the size of a carotid artery in a dog became completely occluded with masses of thrombus, fibrin, and red blood-cells. When, however, heparin was given under similar conditions, the blood-cells, including platelets, could be seen passing the glass window. The platelets would hover in the region of the scratch on the glass and rarely would an occasional one remain for a moment before rushing on again in the flowing stream. The glass cell remained clear for as many hours as the observations

were continued, if heparin was given in sufficient quantities to affect clotting time. When the clotting time was allowed to return to normal, the platelets again accumulated in the glass cell.

From this study by Best, a different appearance of platelets from that ordinarily seen on a stained slide was obtained. In the blood-stream the platelets appeared to be moderately large cells, with multiple finger-like processes extending out from the protoplasm of the cell body. There is a small nucleus, which is probably the only remaining part of the platelet visible on the stained blood-smear on the glass slide.

While Howell's original idea was that heparin would prevent clotting of blood, there is considerable evidence in this work that it will also prevent thrombosis. How it does prevent thrombosis is not known. It is suggested, however, from these experiments, that heparin may have some specific effect on platelets themselves. Whether it affects the stickiness of the platelet, so that it does not adhere to injured surfaces, or whether it affects the cell membrane in such a way that the platelet does not break up and thereby liberate thromboplastic substances, has not been decided.

Large quantities of heparin are liberated in anaphylactic and peptone shock, rendering the blood incoagulable for long periods. The anticoagulant was shown by Jaques[23] to be heparin, as crystalline heparin was isolated from this blood.

Fate of Heparin.—With the assistance of Jaques the rapid disappearance of heparin from the circulation was investigated. Various tissues and the excreta of dogs before and after administration of heparin were assayed for their heparin content. As the original heparin was discovered in liver by Howell, and extracted from lung by Charles and Scott, these tissues were assayed first. No difference in their heparin content was discovered after injections of large amounts of the substance. Normally urine and fæces contain small amounts of an anticoagulant, but this is not increased by intravenous or subcutaneous injection of heparin. Similarly there was no increase in the amount of heparin recovered from kidney, skeletal muscle, heart, or circulating blood after the effect of heparin on the circulating blood had disappeared. There was a slight increase in the spleen under these conditions, but only when the assay was done on the same day as the heparin was injected. The normal storage of blood in the spleen might account for this finding. In several dogs there was an increased amount of heparin recovered from gut.

Yankovsky[24] studied the effects of the removal of viscera on the duration of the action of heparin. His results also indicate that the gastro-intestinal tract takes part in the removal of heparin from the circulation. The possibility of a ferment destroying heparin must be considered, but further work on this aspect of the subject must be done before conclusions can be drawn.

Toxicity.—As it was hoped that heparin might ultimately be used safely in clinical patients, knowledge of its toxicity was a very important matter. The Howell unit of heparin is the amount which will prevent clotting of 1 c.c. of cat's blood for twenty-four hours. As this test is not carefully controlled, it was considered advisable to set up a standard for a unit of heparin. This standard has been set up in the Connaught Laboratories (*Surgery*, 1937, August), in the University of Toronto. The unit in the preparation provided by these laboratories is the potency of 0·01 mg. of the purified crystalline barium salt. This unit has about five times the activity of the original Howell unit.

Using heparin of a potency of 15 units per milligram, Howell and MacDonald[25] injected a sufficient quantity into a dog to render its blood incoagulable. This amount was approximately 0·45 mg. per kilogram. The injection was repeated daily for five days, and no demonstrable change in the red and white blood-counts or in the platelet-count occurred, and there was no deleterious effect on the animal. Reed[26] injected moderate quantities of heparin intravenously in normal and etherized dogs and rabbits, and found no change in temperature, no change in respiration, no concentration of blood-cells, and no cardiovascular effects.

In 1924 Mason,[27] using 5 units per milligram material, added from 50 mg. to 300 mg. to the blood used for transfusing human beings. In about half of the cases various reactions, from slight chills to severe headache, high fever, and nausea, were observed. He concluded that while the more impure form of heparin was too toxic for routine clinical use in doses of 500 units, later preparations gave more encouraging results. Howell reported the use of heparin containing 100 units per milligram in blood transfusions. There was slight reaction in 2 out of 10 transfusions carried out. Godlowski[28] found no evidence of toxicity in patients when he injected 1 mg. of heparin per 10 c.c. of blood. This preparation contained 10 units per milligram.

In our experience, the 5-unit material, which was the only preparation available when these experiments were started, caused marked toxic effects when administered intravenously to dogs. Some of these animals died from the toxic effects. With 15-unit material there were fewer toxic effects, but when doses sufficiently large to raise the clotting time to one hour were administered there were marked toxic effects. There was a fall in blood-pressure, with muscular weakness, vomiting, marked rise in temperature, and prostration. With larger doses there was hematemesis, melæna, and collapse going on to death. Autopsies on these animals showed many petechial hæmorrhages in the mucous membranes, with bleeding into the lumen of the intestine. There were multiple hæmorrhages beneath the serous membranes, including the peritoneum, pleuræ, meninges, and epicardium, and massive hæmorrhages in practically all organs. With the more highly purified heparin, with a potency of 250 units per milligram, no toxic effects were observed when 500 mg. were given intravenously over a period of seventy-two hours.

Further tests for toxicity with this later preparation of heparin were made upon several species of animals. The bloods of these animals, including guinea-pigs, rabbits, and mice, were made incoagulable for fairly long periods of time without toxic effects.

The continued efforts of our colleagues, Charles and Scott,[29] have resulted in a purified crystalline barium salt of heparin with a potency of 500 Howell cat units per milligram. With this material, no toxic effects have been observed in many hundreds of experiments on various animals, including dogs. Doses sufficiently large to raise the clotting time of dogs to four hours have had no toxic effects. There is universal agreement that this highly purified heparin may be injected in large quantities without injurious effects of any kind, and it is agreed that the toxic effects of the older, weaker products were due to impurities and not to heparin itself.

Effect of a Single Injection.—It is well known that a single injection of heparin intravenously is followed within a few minutes by a rapid rise in clotting time. There is a short plateau to this curve, which then descends less rapidly to reach normal levels at intervals depending on the dosage. In *Fig.* 411 an example

of this effect is shown. A dog of 11 kg. was given 2200 units of heparin intravenously. Within ten minutes the clotting time rose from the normal of 2 minutes to 15 minutes. After remaining at that level only a few minutes a gradual return to normal occurred in about one and one-half hours.

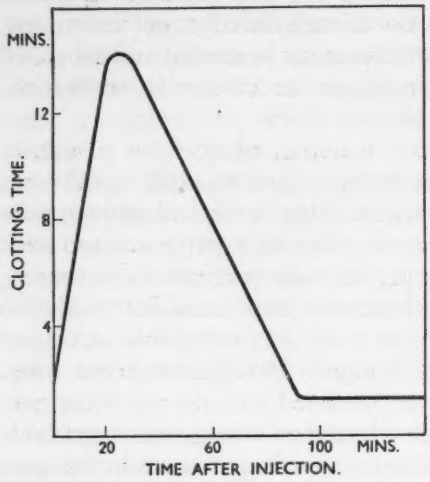

FIG. 411.—Showing the effect on clotting time of a single injection of heparin.

When larger doses are given a longer clotting time is obtained. A limit is ultimately reached when the clotting time is prolonged to about four and one-half to five hours with a dose of 300 units per kilo. Even if the dose is doubled, however, there has been no further increase in clotting time beyond this level.

At this stage it was hoped that a more prolonged effect might be obtained if heparin were combined with some other substance, just as the effect of insulin was prolonged when combined with protamine. It was suggested by the author that protamine be tried with heparin. In the light of the experiments that finally showed the antagonistic action of protamine to heparin, there is little wonder that the desired effect was not obtained.

Negative Phase.—Howell[22] has reported a decrease in clotting time following the primary increase produced by an injection of heparin. In our experiments we did not observe any changes in clotting time, sedimentation rate, leucocyte or erythrocyte counts, or capillary resistance tests. It was concluded from our work to date that there was no evidence which would lead us to suspect a negative phase.

EXPERIMENTAL INVESTIGATIONS

Methods of Administration.—In the preliminary stages of this investigation, heparin was administered in a variety of ways and certain descriptive terms have been used for these.

Local Heparinization.—This is the term used to describe the application of heparin to one particular area. The heparin is mixed in vaseline or jellies of various sorts and is applied in these forms to the edges of divided blood-vessels, or to the field of operation on blood-vessels. The results obtained by this method of administering the anticoagulant were not striking, and there seems to be no occasion in surgery when this method of application would be useful. In this respect the effect the heparin differs rather widely from that obtained by applying hirudin by this method.

Regional Heparinization.—This is the term used to describe the administration of heparin in such a way that the clotting time of the blood in one area is increased without affecting the clotting time of blood in other parts of the circulatory system. This is applied chiefly when surgery on arteries is undertaken. The heparin is injected proximally to the field of operation on the vessel, so that the clotting time in this area is increased, but samples of blood secured at the time from veins other

than those draining the affected area are not changed. With larger doses, obviously more of the anticoagulant reaches the general circulation and a general increase in clotting time is obtained.

General Heparinization.—This describes the results of the administration of heparin into a vein or artery at such a rate that the clotting time of the blood from all parts of the body is increased. While some of the results reported in this paper were secured by regional heparinization, general heparinization was used more frequently.

The heparin was given intravenously by one of four methods.[30] In the early experiments a single intravenous injection was made with a syringe. In the second group the heparin was given by repeated intravenous injections spaced so that each succeeding injection was given before the effect of the preceding one had completely disappeared. When large doses sufficient to change the clotting time to four hours or more were given, the subsequent injection was given before that space of time had elapsed. In a third group the heparin dissolved in saline was given as a continuous injection by means of a motor-driven pump. These experiments were continued for periods up to ten hours, during which time the animals were anæsthetized with nembutal, sodium amytal, ether, etc. The difficulty arising from this method of administration was that the effect of anæsthesia overlapped the effect of heparin, and a true assay of the results was difficult. The method which has been used for the past years and which has been most satisfactory follows the technique developed by Jacobs.[31] By this method continued intravenous infusions may be given to dogs for days or weeks without interfering seriously with their comfort. Under anæsthesia, a small catheter is inserted into the external jugular vein and through this heparin is injected. A system of tubes, with a swivel joint, prevents the animal from becoming tangled in the apparatus. The dog is kept in the usual cage and is quite free to move about, take food, and lie down without discomfort. By carefully adjusting the apparatus the dogs have received continuous intravenous infusions for periods up to two weeks without interruption.

Subcutaneous Injection.—Some change in clotting time has been produced by injecting benzidine heparin subcutaneously. While this method has not given very satisfactory results to date it merits further investigation.

Heparin injected intraperitoneally did not change the blood-clotting time.

Bancroft's[32] suggestion that sodium thiosulphate may stimulate the production of heparin is interesting, as it suggests the possibility that the prevention of thrombosis in future may be effected by injection of a heparinoplastic substance rather than by heparin injection.

Method of Producing Injury to Veins.—To test the effect of heparin on thrombosis and clotting various methods of producing thrombosis in vessels were tried.[33]

a. Mechanical Injury.—The radial and saphenous veins of dogs were exposed under local anæsthesia. A needle carrying a silk thread was passed through the lumen of the vein for ¾ in. and tied loosely (*Fig.* 412). The vein was then crushed severely over the whole length of the segment containing the suture. The thread was withdrawn and the skin closed. The veins were left in situ for periods ranging from seven hours to seven days, following which they were removed and examined.

b. Chemical Injury.—By this method it was hoped that a higher incidence of thrombosis would be obtained. Sodium ricinoleate, which is very irritating to the

intima of veins, was injected in a segment of vein. It was obstructed by digital pressure for a period of three minutes and then released.

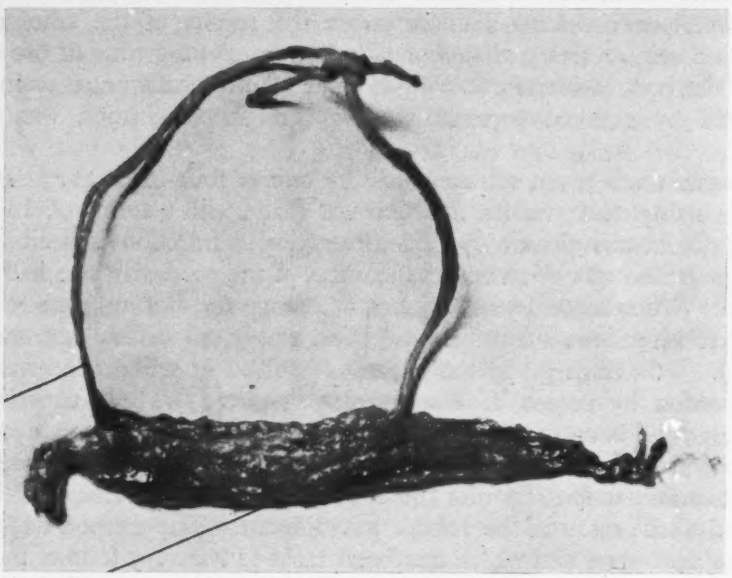

FIG. 412.—Showing the method of placing a suture in the lumen of a peripheral vein to produce thrombosis.

In a large group of control experiments numbering several hundred, over 90 per cent of veins injured by this method were occluded and over 80 per cent were occluded when mechanical injury was used. When heparin was given to animals following similar injuries to their veins, over 80 per cent of the vessels remained patent. To obtain the best results it was necessary to continue the injection of heparin for more than twenty-four hours, during which time the repair processes in the intima of the vessel were well established. If the heparin injection was continued for a sufficiently long time, the vessels healed completely and occlusion did not take place after the injection was stopped.

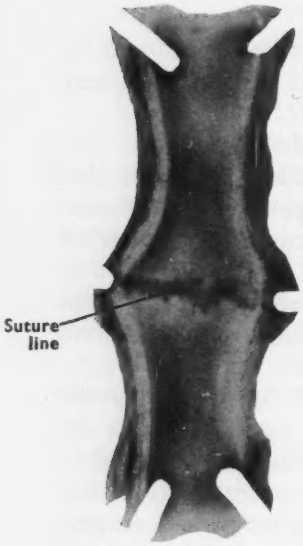

FIG. 413.—Lumen of artery, showing end-to-end suture 3 months before and treatment with heparin. The suture line is healed; there is no thrombus present.

Arterial Anastomosis.—In the excellent work of Carrell[34] an unprecedented technique for anastomosis of blood-vessels has been developed which gives satisfactory healing, the vessel remaining patent. We find, by using a very careful technique on carotid arteries in animals, that a fair number of anastomoses may be carried out with success and that the vessels remain patent. However, by applying less care and doing the anastomoses with ordinary operating-room technique, most of these vessels become occluded by a thrombus at the site of the suture line and this extends into the distal segment. In 50 such experiments

in which regional heparinization was used, the arteries remained patent in 40, or 80 per cent, whereas in the controls only 35 per cent were patent. Later we found when the technique of continued injection of heparin over a longer period of time was improved, that all the anastomoses remained patent, provided the experiment was completely satisfactory and heparin was given continuously for at least seventy-two hours. Examination of these vessels showed that if they remained patent for seventy-two hours there was practically complete healing of the intima across a reasonably good suture line (*Fig.* 413). Our experience showed that it was unlikely that further thrombosis would occur at that site. Specimens recovered a year afterward showed only a slight scar at the site of anastomosis.

Venous Grafts.—In various text-books and articles on blood-vessel surgery, venous grafts are mentioned, but I have been unable to find a report in which a venous graft was used successfully, either experimentally or clinically. One would assume that, as this operation had been advocated, it had been tried, but the fact that I can find no reports of successful cases in the literature referred to would indicate that probably the results were failures. It was thought, therefore, that this operation would provide an excellent test for the effect of either regional or general heparinization.

Segments of carotid arteries in dogs varying from 1 to 3½ in. in length were excised. A similar length of external jugular vein removed from the same animal was anastomosed at both ends to take the place of the artery removed. These

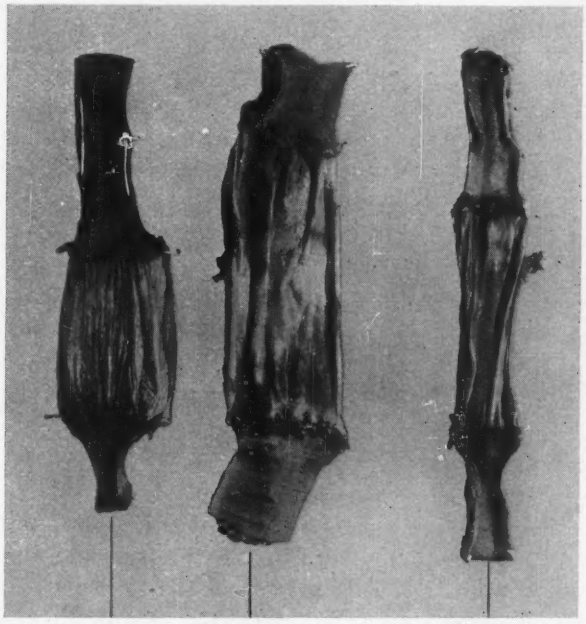

FIG. 414.—Experimental venous grafts removed 8 hours, 24 hours, and 24 hours after grafting and treatment with heparin.

anastomoses were carried out with ordinary operating-room technique without using vaseline or other substances on the suture material or the surfaces of vessels exposed during the operation. An idea of the degree of care used can be inferred

from the fact that to complete the anastomoses at both ends of the graft required a period of from twenty minutes to half an hour.

There was some doubt in the earlier stages of this work whether the thin-walled vein would withstand the high arterial pressure. It was interesting to observe that under the arterial pressure the venous graft ballooned out in a sausage shape and its walls were so thin that eddies of the circulating blood could easily be seen through them. In the early stages we tried to make these structures more secure by applying a double line of sutures, supporting the graft with surrounding tissue, etc. We finally arrived at the conclusion, however, that these measures were unnecessary.

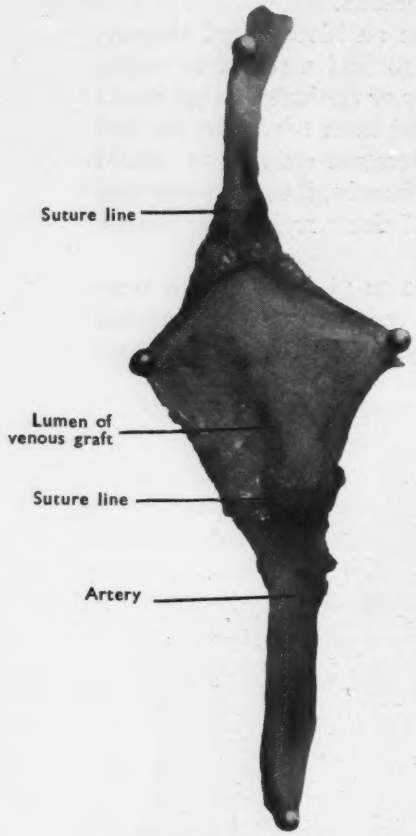

FIG. 415.—Photograph showing perfect healing of suture line between artery and venous graft 8 days after grafting and treatment with heparin.

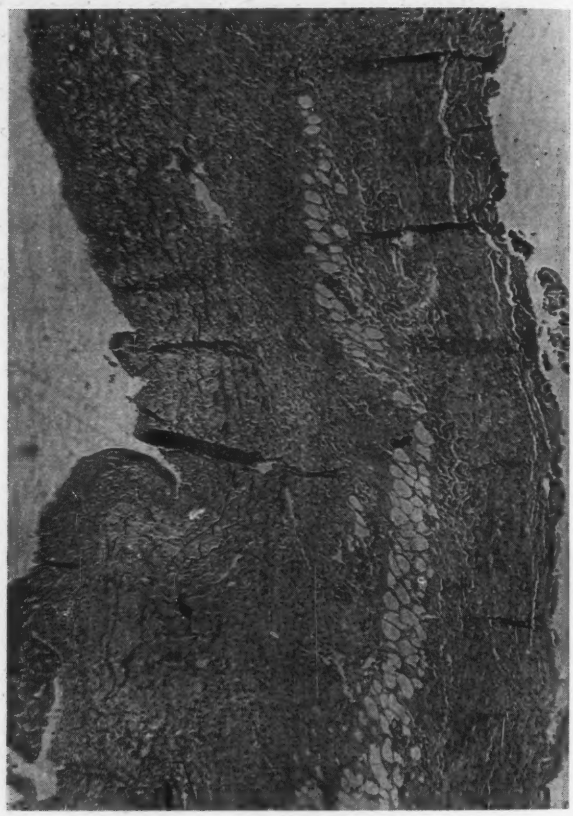

FIG. 416.—Suture line between artery and venous graft removed 9 days after grafting and treatment with heparin.

The whole problem of success or failure depended, not on the giving way of suture lines of the thin-walled vein, but of thrombosis at the suture lines and in the lumen of this large, sausage-shaped graft. We made the mistake in some of the earlier experiments of making the venous graft too short, so that with flexion of the neck to the opposite side the animal would tear one of the suture lines. Since that time, using a greater length of vein as a graft, there have been no more of these disasters. In all the control experiments with these grafts when heparin was not used, the whole area became occluded within a short time with thrombus and blood-clot, and the circulation was stopped. When heparin was given and continued for not

less than seven days, these grafts invariably remained patent (*Figs.* 414–421). There was considerable difficulty in these experiments in continuing heparinization

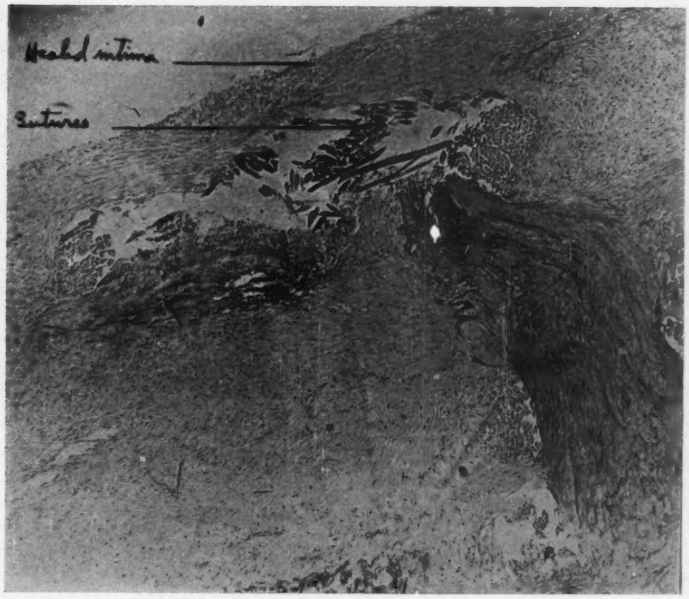

FIG. 417.—Suture line between artery and venous graft removed 23 days after grafting; showing healing of intima, media, and adventitia.

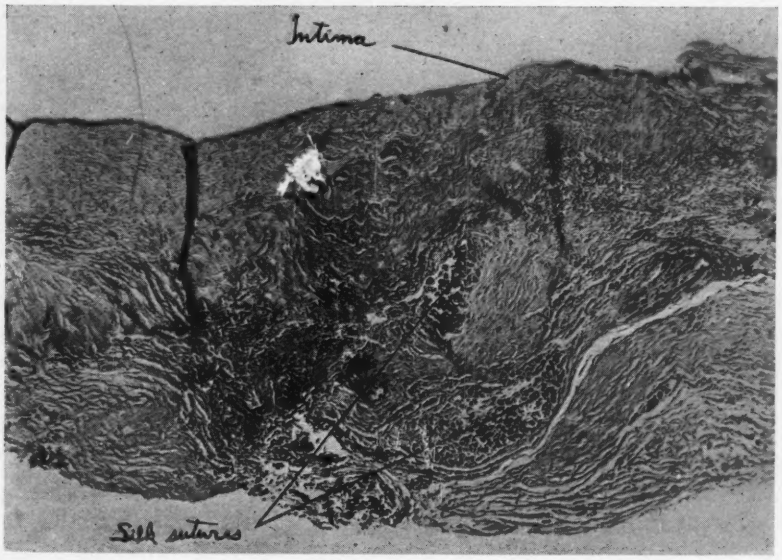

FIG. 418.—Suture line between artery and venous graft removed 42 days after grafting, showing excellent healing of all coats of the vessel, and the increased thickness of the wall of the venous graft. The intima is smooth with no sign of a thrombus.

for this length of time without some interruption, or complications such as pneumonia, inflammation of the wounds, tangling up of the apparatus, etc. When,

however, an experiment was completed with seven days' continuous heparinization, without interruption, all grafts remained patent. Fifty such grafts have been done. Most of them have been exposed by reopening the incision at intervals of three months, and *Fig.* 419 shows drawings of such a graft two hundred and ninety days after the original operation. In the meantime, this graft has been exposed twice and shown to be patent. On the two hundred and ninetieth day following the original operation the graft was exposed and an elliptical piece excised from the distal suture line, including about 8 mm. of graft and of adjacent wall of the artery. This specimen is shown in *Fig.* 420 under low-power magnification. Four other grafts have had similar segments removed for examination. It was most interesting to find that after about four weeks the wall of the venous graft was considerably thicker

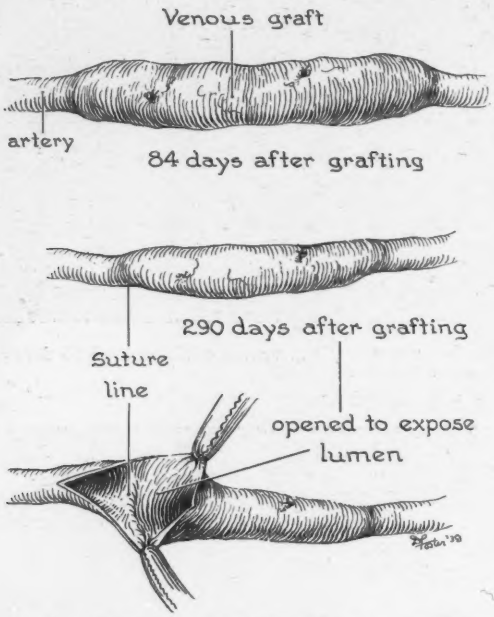

FIG. 419.—Showing 3 in. of external jugular vein grafted into the common carotid artery. The decreasing size of the venous graft is shown at varying intervals until it has an appearance somewhat similar to the adjacent artery.

and more opaque than when it was grafted in originally. Moreover, its lumen had diminished somewhat and the ends of the graft were more fusiform. At six months' interval the wall of this graft was about the same thickness on palpation as the adjacent wall of the carotid artery. It was completely opaque. It had the appearance of a thick fibrous structure with small multiple bleeding points, and resembled the dissected surface of an ordinary scar. It was adherent to all structures surrounding it, but could be dissected off with ease. The wall was tough so that it could be separated without difficulty, and on no occasion was the wall so friable that it was torn during the dissection. All the grafts that we have explored during several months have presented these changes. There has been no evidence of degeneration of the wall, of bulging, or any other change that would indicate that the grafts would not survive. They conducted the blood-stream and pulsated normally, as did the adjacent carotid arteries. The wall was completely compressible, like the wall of the normal artery.

Two specimens removed at intervals are shown in *Fig.* 421. The length of time that each graft was in situ is indicated, and the changes such as the increasing thickness of the wall, with healing of the suture line and diminution of the lumen, are well demonstrated. The intima of the vein appears normal. There is no evidence of degeneration, or of a calcareous

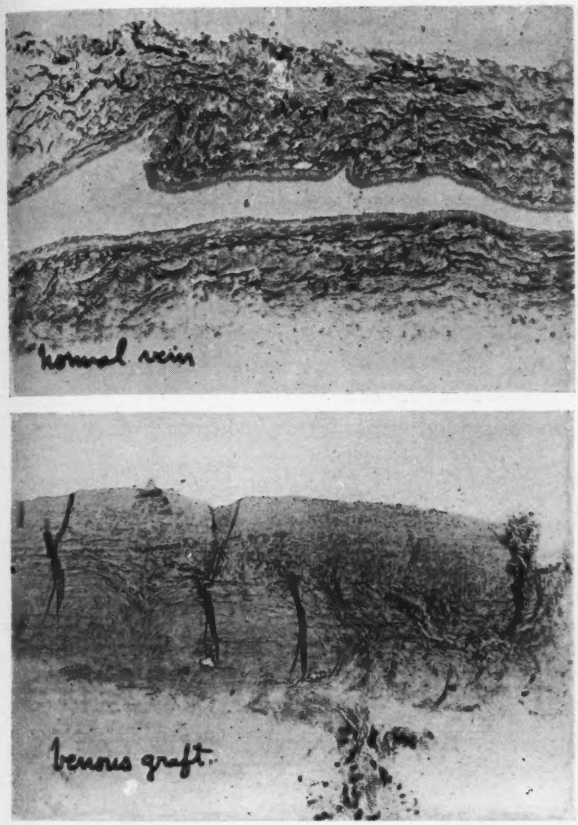

FIG. 420.—Elastic-tissue-stained section of graft shown in preceding figure; *Top*, normal vein. *Below*, section of venous graft removed 290 days following grafting and treatment with heparin. Shows the increased thickness of media and adventitia.

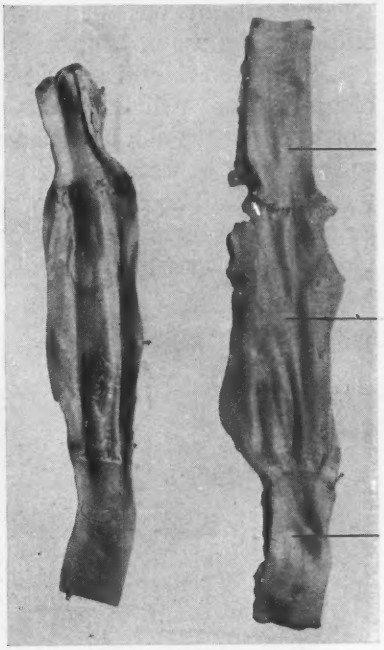

FIG. 421.—Venous grafts removed 23 days (W) and 42 days (X) after grafting. Note the thickness of the venous graft and the diminished lumen at 42 days compared with that at 23 days.

deposit, and after many months the interior of the graft is very similar to the intima of the adjacent carotid artery. The suture lines have healed perfectly without stenosis.

In this group of experiments general heparinization was carried out after the method described by Jacobs.

Embolectomy.—Since Einer Key[35] performed the first successful embolectomy in 1911, a controversy has raged over the correct method of treating peripheral arterial embolisms. The resurrection by Reid and Hermann of the principal of positive- and negative-pressure treatment for impaired circulation, which was used in the British Army in the nineteenth century by one of my surgeon progenitors, has introduced another excellent adjuvant of conservative treatment of these lesions. There are conditions under which conservative treatment with the use of the Pavaex boot is ideal. In other circumstances, however, when the patient is seen early after embolism has occurred, the logical form of treatment would seem to be

immediate removal of the embolus. The chief handicap to this form of treatment and one which provides the strongest argument for those in favour of the conservative treatment, is that not infrequently the site at which the embolus is lodged, as well as the point at which the vessel is opened, becomes thrombosed again. With experimental proof that heparin would prevent thrombosis and clotting, there was great promise that it might be an agent which would entirely change the prospects of these operations by keeping the lumen of the vessel patent after the embolus was removed.

Experiments on blood-vessels in dogs were carried out to investigate the possibilities of the use of heparin in embolectomy.[36]

The femoral and carotid vessels in dogs were opened and a plug of catgut, blood-clot, or small fragments of sponge with blood-clot were pushed along the artery to the next branch so that the plug would remain in place, and the vessel was closed. These plugs were left in place for periods up to three days. After the plug has been in place for six hours, the lack of reaction in the wall of the vessel, with the intima intact and normal, and the lack of adhesion of the clot to the wall, is quite obvious. After twenty-four hours, however, there is a considerable change in the wall of the vessel which contains the clot. There is adhesion of the clot to the wall of the surrounding vessel. At forty-eight hours there are gross changes which can be seen, and under the microscope the wall of the vessel, as well as the contained clot, are invaded quite widely by leucocytes. The clot is firmly adherent to the wall of the vessel, and appears as if it could be separated only by actually scraping it off (*Fig.* 422).

FIG. 422.—Showing the intense inflammatory reaction in the arterial wall surrounding an experimental embolus which has been in situ for 48 hours.

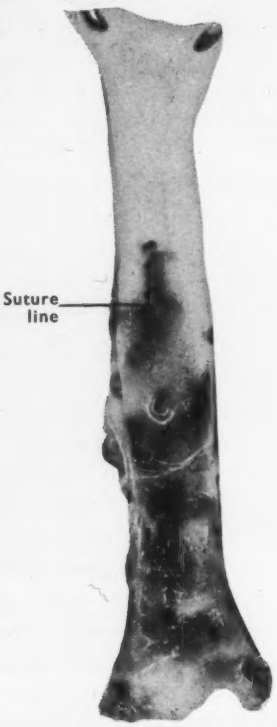

FIG. 423.—Lumen of carotid artery showing healing following experimental embolectomy and treatment with heparin.

After forty-eight hours the vessel was opened through another incision and the plug removed with forceps and a dull curette. The open vessel was filled between

clamps with heparin solution, and the opening sutured. The animal was given continuous heparin injections for the following seventy-two hours. In eight animals in which this procedure was carried out and heparin was given, the vessels remained patent in all. *Fig.* 423 shows such a vessel removed several weeks after this procedure. It demonstrates that the wall has healed perfectly, the two suture lines showing no evidence of weakness or tendency to aneurysm formation. The walls are normal, apart from some staining from blood-pigments. In eight other control experiments when a similar procedure was carried out and heparin was not given, the vessels became plugged again very rapidly.

This was very satisfactory evidence that heparin might be of great value in operations on peripheral arteries, especially those for removing emboli.

Effect of Heparin on Portal Thrombosis.—Theoretically there should be no reason why clotting or thrombosis in the portal circulation should differ from that in the systemic circulation. As there is some difference in the chemical constituents of the two blood systems, it was decided that investigation of the effect of heparin on the portal system might be worth while. This was of special interest because of the clinical observation that splenectomy in the human being is frequently followed by extensive portal thrombosis and death. If heparin had a similar effect in this circulation to that observed in the general circulation, it was possible it might be of value following operations of this nature.

In nine dogs the splenic vein was injured in a similar fashion to that described for injury of superficial veins. The spleen was removed at the same operation. After seven days the animals were operated upon again and the splenic vessels removed for examination. In eight animals a similar procedure was carried out, and immediately following the operation continuous intravenous injections of heparin were instituted for periods varying between three and seven days. The animals were operated upon one week after heparin was stopped and the splenic vessels were removed for examination.

In the nine animals in which heparin was not given, seven splenic veins were thrombosed throughout their whole length. Of the eight animals given heparin, the splenic vein was patent in all, and the suture which was left in the lumen of the vessel was either lying free or was incorporated in a scar on the wall.

This was fairly satisfactory evidence that heparin is effective in the portal circulation and prevents thrombosis as it does in the peripheral circulation.

Transplantation of Organs.—Organs have been successfully transplanted by the beautiful technique developed by Carrell. It was decided to investigate the possibilities of this procedure by using heparin to assist in keeping the circulation patent. Kidneys of dogs were excised and the renal vessels anastomosed to the common carotid and external jugular vein in the neck. The kidney was placed deep to the sternomastoid muscle in some and just beneath the skin in others. The animals were heparinized. In our hands, using ordinary surgical technique, the results were much better when heparin was used. Further work on this aspect of the subject is in progress at the present time and a report thereon will appear later. While the kidney tissue was far from normal, it was still viable and was secreting urine.

Extra-corporeal Loop.—While the effect of heparin on platelets in blood-vessels preventing thrombosis has been proven, visual evidence of this process in action has been demonstrated best by the extra-corporeal loop described

by Shionoya.[37] A transparent tube of cellophane was placed as a communication between the common carotid artery and the external jugular vein in animals. Through this transparent membrane the circulating blood is easily seen. Under ordinary conditions, within a few minutes small white specks appear downstream from irregularities in the tube. These enlarge at such a rate that within the space of an hour, more or less, the tube is plugged with thrombus. Blood-clot rapidly forms, in relation to the enlarging thrombus. Best and McLean[38] have repeated these experiments many times, and have been impressed with the rapidity with which these transparent conducting tubes become plugged. When heparin was given, the results were altered very noticeably. The tubes remained patent as long as sufficient heparin was given to increase the clotting time of the animals' blood.

Coronary Occlusion in Animals.—Further evidence of the ability of heparin to prevent thrombosis was demonstrated by a parallel series of experiments on coronary arteries. Sclerosing solutions were injected into the artery, and in other experiments into the tissues surrounding the artery. Without heparin these vessels regularly became thrombosed, but Best and Solandt[39] found that continued injections of heparin would prevent occlusion.

Mural Thrombosis.—Further work by Best and Solandt showed that when an infarct was produced in the wall of a heart, a mural thrombus formed in the cavity of the heart. A mass the size of a small cherry may form within a period of about an hour or less. This has a fairly firm attachment to the infarcted area, and spreads out first in a sessile fashion and later on as a pedunculated mass. When a continuous injection of heparin sufficient to raise the clotting time is administered these mural thrombi do not form.

CLINICAL APPLICATIONS

The experimental work on heparin was started with the hope that a preparation of heparin and a technique of administering it might be developed to improve the treatment of diseases where thrombosis in blood-vessels was an unsolved factor. There is a large group of diseases in which spontaneous thrombosis of venous and arterial systems occur. These frequently are followed by complications such as embolism, resulting in the devitalization of tissue and often going on to gangrene. There is also an important group in which pulmonary embolism resulting from thrombosing processes results in sudden death, and in others in prolonged serious illness with persisting disability. There is another group of diseases in which the surgeon's best efforts are frequently unsuccessful because of thrombosis, where a direct operative attack is made on blood-vessels, such as the surgical treatment of aneurysms, invasion of important vessels by tumour, or other diseases requiring ligation of vessels, e.g., the common carotid and internal carotid arteries.

With excellent experimental evidence proving that heparin will prevent thrombosis and clotting, the day arrived when we considered we were ready to attempt its use in clinical patients. Former attempts at using heparin in patients were made mostly in blood transfusions. Mason, McClure, and many others found that heparin was too toxic to be of practical use. We[40] felt, however, that with a substance which was non-toxic in animals and which was much more potent than that used by former workers, a clinical trial should be made. Consequently, on April 16, 1937, in a clinical case a needle was passed into the lumen of the brachial

artery and with a motor-driven pump a solution of heparin in saline was given. The heparin used on this occasion had a potency of 250 units per milligram. The rate of injection was increased until samples of blood collected from the median cubital vein in this arm showed an increase of clotting time reaching fifteen minutes. The injection was continued for two hours and then stopped. Within half an hour of stopping the injection, the clotting time of the blood returning from this extremity was normal. During the period of injection there was no change in the clotting time of the samples of blood removed from the veins of the other extremities of this patient. No toxic effects were observed.

Encouraged by this experiment, other patients were given heparin intravenously in sufficient quantities to increase the clotting time of the blood in the general circulation to fifteen minutes. In 5 of 9 patients so treated, there were fairly marked toxic effects. These took the form of severe headache, chills, early marked collapse with pallor, rapid pulse, and dyspnœa. These effects were followed very shortly by a high fever and general malaise. The whole clinical picture of this reaction resembled very closely the effect produced by ordinary protein shock. When heparin was discontinued early, during this reaction, the symptoms were of short duration and within twenty-four hours the patient returned to normal.

These toxic effects were very disappointing, but probably fulfilled a useful purpose in stimulating further efforts in the purification of heparin. When our results had been explained to Charles and Scott, they continued their work on purification. Ultimately they succeeded in preparing a crystalline barium salt with a potency which was double that used in the first patient. One milligram had the activity of 500 Howell cat units. With each stage of purification, further clinical tests were made, but it was not until the final crystalline product, apparently the pure form of heparin, was obtained, that the toxic effects disappeared. We continued testing on patients the toxicity of this purified form of heparin. Increasing doses were given over longer periods of time, until on more than one occasion clotting times of an hour and a half were reached. In several cases injection was continued for several weeks, the longest one lasting forty days continuously, during which time the patient received 600,000 units of heparin. Following another operation within four months on this particular patient, heparin was administered again. It was interesting to observe that there was no anaphylactic reaction produced by heparin. In more than 400 clinical cases there have been no toxic effects from this purified form of heparin.

Venous Thrombosis.—In an attempt to discover indications for and contraindications to the use of heparin, the clinical applications of many of the experiments which were done on animals were used when suitable clinical cases were found. It was possible that, even though heparin will prevent thrombosis in animals, it might have a different reaction in human beings. It was with great satisfaction, therefore, that we observed, as the number of clinical cases increased, that there was no thrombosis of the vein in which the intravenous injection of heparin had been made by means of a steel needle. As these injections were continued, on many occasions through a needle at the same site in the same vein for periods up to two weeks, not infrequently there was a reaction with mild cellulitis about the needle, occasionally with lymphangitis. When the needle was removed, the cellulitis rapidly disappeared, and on all occasions the vein was not thrombosed and the inflammation subsided rapidly. It was easy to demonstrate that the vein was patent.

On several occasions after the needle had remained in one spot in the vein for periods of from ten days to two weeks, it was removed because of these skin reactions, and placed in the same vein at a spot a few inches more distally and the injection continued for a week or more at that site without thrombosis in the vessels. This in itself in more than 400 clinical cases was fairly satisfactory evidence of the effect of heparin in preventing thrombosis. Under ordinary conditions, in our hands, a steel needle lying in a vein caused sufficient irritation when saline or glucose solution was injected to cause occlusion of the vessel within a few days.

Embolectomy.—With the experimental evidence that heparin might assist in obtaining results in embolectomy, especially in cases in which operations were not done for several hours after the embolism occurred, it was decided to try it on some clinical cases. Embolectomy has been successful in the hands of many surgeons when it is done within a few hours of the lodgement of the embolus. Even though the embolus is removed early, however, not infrequently the operation is a failure. Because of the weakened condition of the patient with chronic heart disease, low blood-pressure, or high venous pressure with stasis, recurring thrombosis may occur at the area from which the embolus was removed or at the suture line. In cases where the operation is not done for a period of ten hours or more following the embolism, the prospects of a good result are increasingly bad with the lapse of time. After twenty-four hours very few cases are successful.

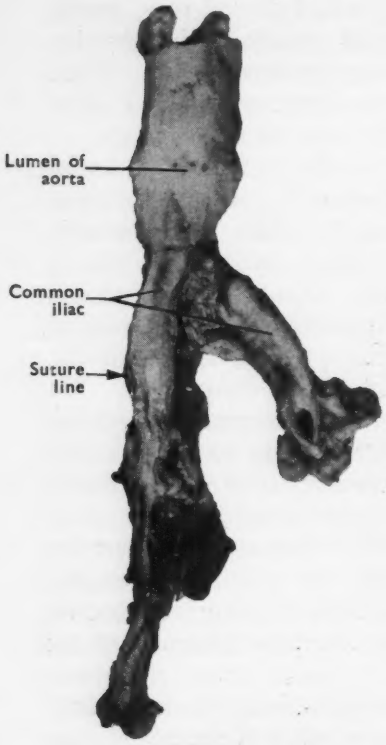

FIG. 424.—Lumen of aorta and common iliac arteries where an embolus was lodged for twenty-five hours before it was removed. The specimen was recovered 16 days later. The suture line is healed and the lumen is clear, following treatment with heparin in a clinical case.

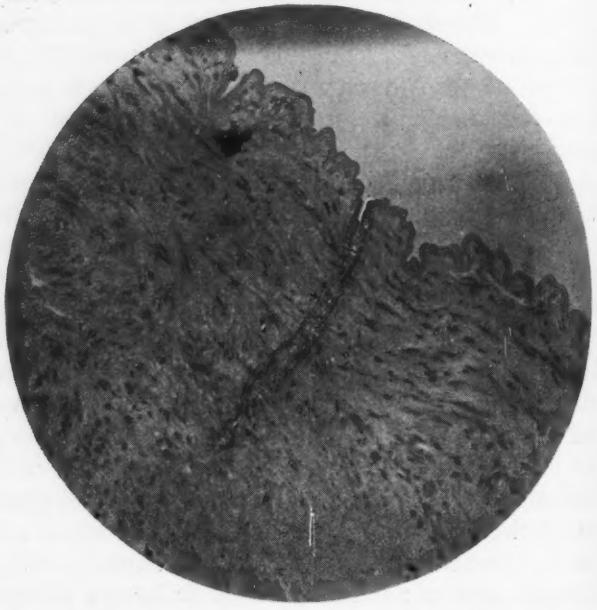

FIG. 425.—High-power view of incision through which embolus was removed, showing perfect healing with no thrombus formation following treatment with heparin.

Since heparin has been available, 12 arterial embolectomies have been done[41] successfully. If the lumen was completely cleared of the plug and the circulation

restored, all the cases were successful when treated with heparin. This drug was introduced into the vessel at the time of operation and the patient was heparinized for from three to fourteen days following. In all these the vessel has remained patent and circulation has been satisfactory in the extremity.

We have been fortunate, speaking only from the scientific point of view, in being able to obtain two of these specimens of arteries which have been operated upon. One was a case in which a subsequent autopsy enabled us to examine the arteries and to see that a complete restoration of the circulation had taken place. This was a patient who was operated upon twenty-five hours after the first appearance of symptoms for embolism involving both common iliac and femoral arteries. The emboli were removed, but they did not slip out as easily as in the earlier stages of

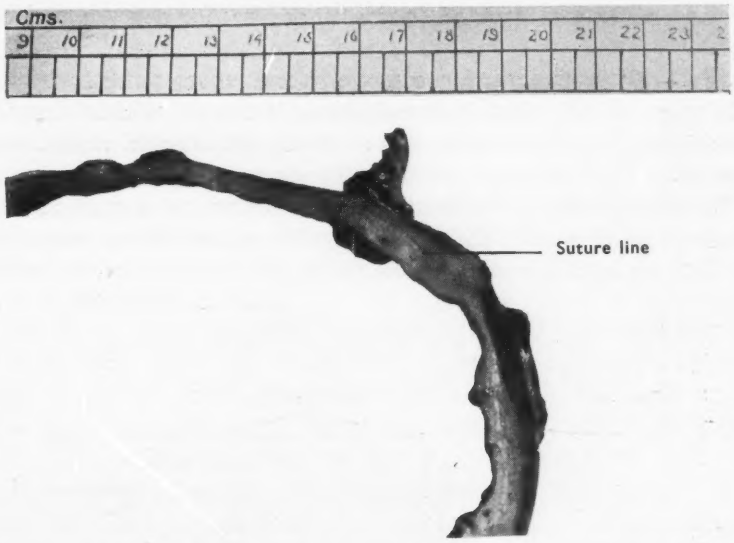

FIG. 426.—Showing lumen of common and external iliac and femoral arteries of a clinical case, recovered twenty-four hours after embolectomy. The lumen is clear, and the suture line is healing, with no sign of thrombus formation, following treatment with heparin.

the disease because of some stickiness of the intima. Before the arterial clamps were removed from the arteries these were filled with a heparin solution. When the clamps were removed, the circulation returned quickly to both feet. From then on the patient's blood-clotting time was kept above twenty minutes for two weeks, and then the heparin was discontinued. The circulation remained normal and there were no ill-effects apart from a moderate-sized hæmatoma in the abdominal incision, which caused no special trouble. However, in the left foot, even though the palpable pulsations in the anterior and posterior tibial arteries remained normal, there was some residual anæsthesia and loss of motion, which were nearly complete at first, but showed daily improvement. At the end of the second week the foot was well on the way to recovery. This was interesting because of the fact that the circulation was restored and maintained in a leg and foot that had been cut off from its source of nourishment for a sufficient length of time to cause some of the tissues to be seriously damaged. On the fifteenth day post-operatively the patient died of other lesions. The aorta and iliac and femoral arteries were recovered. The vessels were all perfectly clear, with not the slightest sign of thrombosis or blood-clot,

either on the areas from which the emboli were removed or at the incision. The latter was healed so perfectly that it could not be found on the intima surface except by a very careful search. In another case which died of other embolisms about twenty-four hours after embolectomy, the vessel, including the operative field, was recovered. The patient had been given heparin until just before death. The vessel showed no sign of thrombosis and the suture line was intact, with no evidence of thrombosis about it. (*Figs.* 424–426.)

While a certain number of cases of peripheral embolisms are incomplete, and others have sufficient collateral circulation to survive, many develop gangrene of the extremity necessitating amputation. From our experience with the use of heparin in this operation, one is encouraged to believe that many more cases may be saved amputations. The results of operations on many of the later cases in which embolectomy formerly was doomed to failure are good when the patient is treated with heparin.

Phlebitis.—When looking for cases in which to test the toxicity of heparin during early stages of this clinical investigation, it was considered that several cases of thrombophlebitis which were on the wards at the hospital might benefit by an intravenous saline injection, and incidentally we might gain some information on heparin. We were greatly surprised to find that there was a marked change in the clinical course of these cases. This encouraged us to treat more cases of this disease, until up to date we have treated 50 cases under carefully controlled conditions. We

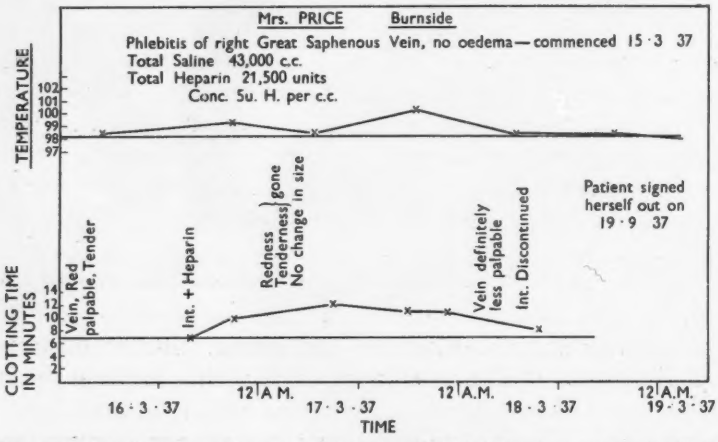

FIG. 427.—Showing the course of a case of thrombophlebitis following treatment with heparin.

have been impressed that in this group of cases all received some beneficial effect. Within a few hours the symptoms were much improved. The pain of which the patient complained was diminishing or had disappeared. The temperature showed a tendency to fall, and over the next few days had a fairly rapid fall to normal. The swelling and œdema began to recede rapidly (*Fig.* 427). While it is too early to be able to judge the end-results of these cases, so far in this group there has been less persisting œdema than one expects in this disease generally. Pulmonary embolism, which is a common complication, occurring in 15 per cent of 600 cases, did not occur in this group treated with heparin.

Unquestionably there is a considerable difference in cases of thrombophlebitis. Those in which thrombi occur in varicose veins probably have a different origin

from the massive single or bilateral thrombophlebitis commonly known as phlegmasia alba dolens. A few of our cases had thrombosis in varicose veins, but most of them were patients who were quite ill with high fever and œdema of the legs, the swelling extending over the lower abdomen. Five of these cases were of the migrating type of thrombophlebitis. The effect of heparin was most noticeable when a case was seen very early in the development of the disease. It was equally effective in cases of thrombosis in superficial varicosities and deep thrombophlebitis with massive œdema. The early effects and final results have both been better than we expected in both these groups. In the cases of migrating thrombophlebitis the acute symptoms subsided fairly rapidly, as in the other groups. Three of these, however, have had a recurrence of the phlebitis, which is characteristic of the disease. Of course there is no reason why heparin should remove the cause of the migrating thrombophlebitis, and therefore it could have no effect in preventing recurrences. In the other forms of thrombophlebitis it has been our hope that if further extension of thrombosis could be prevented with heparin, the existing thrombus would become attached to the wall of the vein and complications such as embolism might not occur. Many of these lesions develop in patients who are in bed with acute illnesses, or following operations. It was hoped that if the extension of thrombosis could be prevented until the patient recovered from the illness and was able to be about actively, the cause for the original thrombosis would disappear and a cure would result. So far in more than two years we have had no recurrences in the cases of massive thrombophlebitis.

One is uncertain what the factors are which caused the improvement in this disease. Possibly the symptoms, with swelling and œdema, are caused by the inflammatory reaction excited by the local thrombosis, as described by Homans.[42] Looking for a theory to fit the facts, one is impressed that with heparin limiting the progressive thrombosis, the inflammatory reaction to the thrombus already present may burn itself out fairly quickly and the symptoms subside. Coincidentally, with no further thrombus present to excite further inflammation, the patient recovers rapidly. Why the pain should be relieved within a few hours is unknown. It would seem that this must be the result of relieving spasm of the vein, but proof of this is lacking so far. Unquestionably infection plays a part in some cases of thrombophlebitis, but as cases of all types have responded, we have not attempted to classify or explain the results. It is possible that the continuing thrombosis is a factor common to all cases.

The average case of acute thrombophlebitis has been treated with heparin continuously for about ten days. In some cases it was continued for a somewhat longer period before the temperature returned to normal. After the first three or four days we encourage the patient to move about actively in bed, and after about two days more we insist on active exercise in preparation for getting the patient out of bed. This latter event occurs on the average between the tenth and twelfth days. The patient is encouraged to exercise actively out of bed and develop muscle. If there is no recurrence of symptoms the heparin injection is stopped, and the patient is discharged from the hospital.

Obviously in human beings it is impossible to control a group of experiments as one does in the laboratory, and for that reason our evidence on the effect of heparin on thrombophlebitis is open to criticism. It is true that many cases of thrombophlebitis subside rapidly of their own accord and undoubtedly that would

have happened in a fair number of our cases. However, the results are spectacular compared with those of cases of thrombophlebitis which, prior to the recent vogue of early exercise, were confined to bed for many weeks or months, with long periods of invalidism. Whether heparin had a specific effect on these patients or not is difficult to determine, but they have been returned to normal activity in a shorter time than the average of a much larger group treated by the accepted methods.

Thrombosis and Pulmonary Embolism.—While the treatment of thrombophlebitis under ordinary conditions has been relatively ineffective, the treatment of its worst complication, pulmonary embolism, had baffled all efforts until Trendelenburg[43] and others used the operation of pulmonary embolectomy. Errors in diagnosis and the short space of time during which an operation must be performed in a dying patient are factors too difficult to overcome, making it unlikely that this operation will ever be the solution to the problem.

The statement is prevalent in text-books and writings on the subject, that pulmonary embolism rarely occurs when there are clinical signs of thrombophlebitis. In 300 cases in the Toronto General Hospital, however, these clinical signs were present in about 15 per cent of cases with embolism. One is impressed with the fact that pulmonary embolism is probably the strongest evidence of thrombophlebitis, and therefore its presence must be admitted even though peripheral evidence is lacking, provided the heart is normal.

In spite of the overwhelming odds against heparin having any beneficial effect, it was decided because of the importance of this problem and the fact that other methods of treatment are mostly palliative, to try a group of these cases with heparin intravenously. It was realized that in a case which has had one or more pulmonary infarctions, almost certainly other thrombi are already present in the venous system, ready to become detached and produce further embolisms. There is no reason why further embolisms should not occur, even though heparin might prevent extension of the thrombus already present. These cases were treated with a full appreciation of these facts, and it was fully expected that heparin would fail to prevent death from pulmonary embolism. Up to the present time 22 cases have been treated. These cases have all had massive pulmonary embolisms producing the usual clinical picture of the disease, with sudden onset, marked collapse, rapid pulse, blood in the sputum, etc. Several of the cases, as is common in the disease, had multiple embolisms with infarcts which were demonstrated on clinical and X-ray examination. Heparin was started at intervals of a few hours to several days after one of these attacks. Again we were surprised and pleased with the results. Of the 22 cases none have died of embolism even though death seemed imminent for some. In this disease also, it is impossible to predict the outcome of a case, as it is well known that 80 per cent of cases of pulmonary embolism survive. In our group some were of a most serious nature, with recurring embolisms, and, to judge from one's previous experience, were of the type in which the prognosis was extremely bad. It is impossible to assess the psychic effect of some form of active treatment in patients who are so ill and anxious as these patients are, but within a few hours there was marked clinical improvement. The dyspnœa and distress, with a catch in the respiration from the associated pleurisy over the infarct, showed rapid improvement. Within twenty-four hours all these patients stated frankly that they were improved. From that time the symptoms rapidly disappeared. In those cases in which there was clinical thrombophlebitis the symptoms of this disease showed rapid improvement

also. With one possible, but unproven, exception, none of these patients had further embolisms. (*Fig.* 428.)

The same principles of treatment were carried out in this group as in the cases of uncomplicated thrombophlebitis. The patients were encouraged to exercise early, and were allowed out of bed after a period of from ten days to two weeks. With the one possible exception already mentioned, none of these cases had any further accidents related to the thrombophlebitis or embolism.

Two of these patients who had pulmonary embolism and were treated with heparin died, and post-mortem examinations were made. One was a case of complete gastrectomy in which the spleen was removed to facilitate the operation.

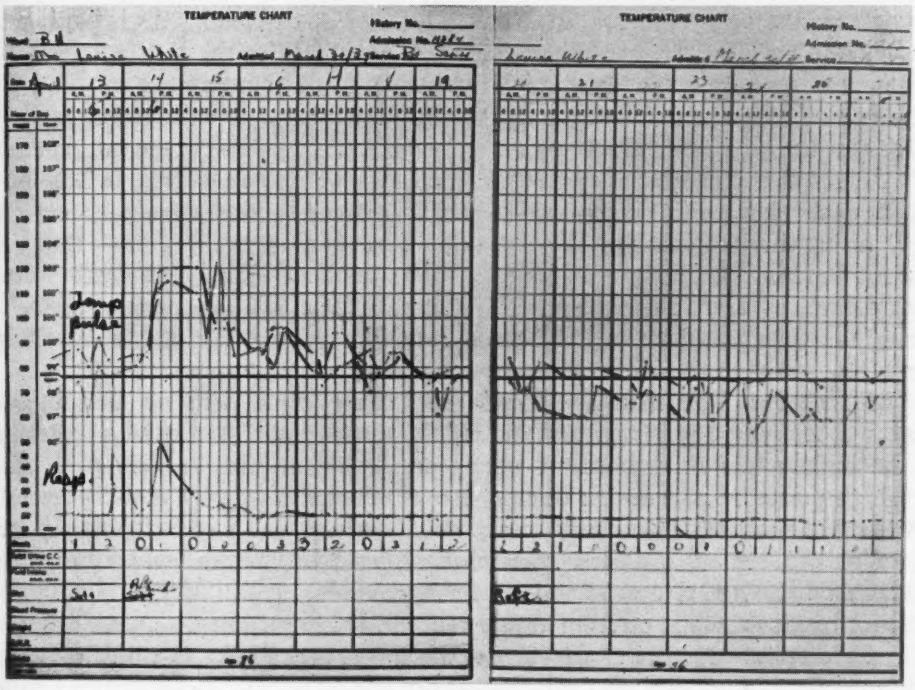

FIG. 428.—Clinical chart of course of typical case of massive pulmonary embolism, following treatment with heparin.

The patient developed thrombophlebitis and pulmonary embolism toward the end of the first post-operative week. Heparin was administered for several days. Post-mortem examination showed there was general peritonitis, which was obviously the cause of death. The infarcts in the lungs were resolving and there was no recent clot or thrombus either in the pulmonary vessels or in the peripheral venous system. An area in the left common external iliac and femoral veins, which was obviously the site from which the embolus had become detached, showed some remaining thrombus. This was firmly attached to the wall of the vein. The second case was one of a young male who had been operated upon for appendicitis and who during convalescence had developed repeated massive pulmonary embolisms over a period of four weeks. The patient lost a great deal of weight, his general health was failing rapidly, and there was a great deal of infarction of both lungs, with extreme respiratory distress and high fever. After heparin injections were given there was rapid

improvement, and within about two and a half weeks he was allowed out of bed. He finally made an excellent recovery, without further accidents. During the next few months he gained strength and weight, and his general health was excellent. On returning to work he rather suddenly developed an acute attack of small-bowel obstruction, for which he was operated upon. Because of his history of repeated pulmonary embolisms, the surgeon requested that he be given heparin following his operation. It was discovered at this last operation that the patient had a duodenal ulcer and there was some evidence of recent bleeding from it. On discussing this with the surgeon it was thought necessary to decide if active bleeding was going on at the present time. This of course would be an absolute contra-indication for the administration of heparin. A stomach tube was passed and several samples of gastric contents were obtained, in which there was gross blood. As heparin would only cause this bleeding to continue, it was stopped before the clotting time of the patient had been affected, so that this patient was not heparinized on the second occasion. The patient died some days later. At post-mortem examination it was found that he had recent massive pulmonary embolisms which were the cause of death.

This is a case in which heparin was used, probably to advantage, in helping the patient recover from thrombophlebitis and repeated pulmonary embolisms. However, during the second illness some months later, requiring an operation, the patient was not heparinized because of bleeding from a duodenal ulcer. As death occurred from pulmonary embolism, one must assume that the effect of heparin is active only during the time in which the patient is receiving it, and that it has no effect in preventing recurrence of thrombosis or embolism.

Mesenteric Thrombosis.—While the cause of mesenteric thrombosis is unknown, it seemed apparent that one of the most important pathological changes in the disease was thrombosis of either mesenteric arteries or veins. With the very high mortality-rate in this disease, it was felt that if heparin could prevent the spreading of thrombosis and gangrene it would be an excellent test for the effectiveness of this substance. In these cases of mesenteric thrombosis several feet of small and large bowel were resected because of gangrene (*Fig.* 429). In the opinion of the surgeons operating none of them would recover, judging from their past experience with the disease. Heparin was started during or soon after the operations, and continued for varying periods up to two weeks. The first 4 cases recovered without complications and are alive and well to-day. The fifth was one in which the diagnosis was made very late in the disease and the patient died about twenty-four hours after resection of the bowel. At post-mortem examination there was no extension of gangrene and the peritoneal cavity was normal. This patient died of bilateral bronchopneumonia. The sixth case was one in which 7 ft. of terminal ileum, cæcum, ascending colon, and hepatic flexure were resected because of extensive gangrene involving this area. At the time of operation the bowel was greyish in colour and stinking, and it was feared that the peritoneal cavity was infected already from this gangrenous bowel. A side-to-side anastomosis was carried out and heparin was given on the operating table. The patient died nine days later. Post-mortem examination showed general peritonitis which, from the reaction in the peritoneum, appeared to be of considerable duration. There was no extension of gangrene in the bowel. It was concluded by the pathologist that there was no recent sudden perforation to account for the generalized peritonitis. In his opinion this peritonitis probably resulted from the presence of gangrenous bowel before operation.

In the opinion of many surgeons, and from the literature on the subject. the mortality-rate in this disease is between 85 and 95 per cent. Most surgeons have never seen a case requiring resection of the bowel recover. In the face of these odds, it probably is a significant fact that the first 4 cases recovered without complications and are still alive and well. The next 2 cases had no further gangrene of

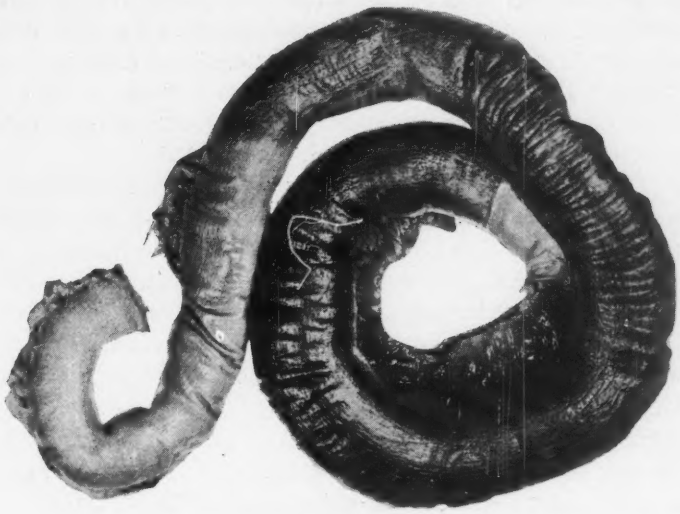

FIG. 429.—Specimen of gangrenous small bowel resected.

bowel and died of other complications. Of all the clinical tests to which heparin has been put, this one is probably the most severe, and one is glad to report that the results have been most satisfactory.

Splenectomy.—The experiments on the effects of heparin in the portal system were so satisfactory that it was thought that cases of splenectomy in human beings might obtain better results with the use of heparin. Certain diseases such as familial jaundice for which splenectomy is done have a fatal outcome in a high percentage because of extensive portal thrombosis following the operation. We have a group of 8 cases in which splenectomy was done. In 3 of these the operations were done for familial jaundice; all these cases recovered without complications and are well to date. In the remaining group the spleen was removed to facilitate the operation of complete gastrectomy; 3 of these patients survived and are well, and 2 died. At post-mortem examination in both cases there was no portal thrombosis.

Obviously conclusions cannot be drawn from such a small group of cases. Most cases of splenectomy survive, and probably these would have survived also, so that one is not justified in drawing any conclusions from the effect of heparin in this group. We propose to continue treating this type of case so that we may increase our information on this subject.

Coronary Thrombosis.—We had hoped to treat a group of coronary thrombosis cases during the early stages of the disease to see if heparin might prevent the extension of thrombosis in coronary vessels, and possibly by that means prevent recurring attacks which are so common in cases that survive the first attack. Unfortunately only a few cases have been available. From these one is reluctant to draw

conclusions. However, some interesting effects have been noted which would encourage further investigation. From the experimental results with this artificially produced lesion, there is some prospect of heparin preventing the complication of mural thrombosis, and thereby preventing either peripheral embolism from the left side of the heart or pulmonary embolism from the right side. It is true that this complication occurs in not more than 10 per cent of coronary cases, but in those, if this complication could be prevented, heparin would be serving a very useful purpose.

We are also treating some cases of *subacute bacterial endocarditis*, hoping that heparin may prevent the extension of the thrombosis in the cardiac valves. This might allow some of the sulphpyradine drugs to sterilize the blood-stream, and in the absence of further thrombosis a cure might be effected.

Cerebral Thrombosis.—The possibility of heparin preventing the extension of thrombosis in cerebral vessels has been considered, but no cases of this nature have been treated.

Venous Grafts.—There are certain accidents and pathological lesions in which major arterial trunks are either torn or interrupted by pressure or thrombosis. Occasionally under such conditions end-to-end sutures of the arteries have been performed satisfactorily, but usually these trunks have been ligated. Not infrequently disastrous results follow such procedures. When an internal carotid artery requires ligation, frequently hemiplegia follows. In cases when major trunks to the extremities, especially to the leg, are ligated or obstructed, gangrene not infrequently supervenes. The experiments with venous grafts in arteries were so satisfactory in animals that it was thought that they might be applied in human beings. It was proposed, therefore, when lesions producing or requiring interruption of the accessible main arterial trunks occurred, that the necessary segments of vessels should be resected and replaced by a venous graft.

We were fortunate about six months ago in having a case of popliteal aneurysm. The swelling was enlarging rapidly and had burrowed through the popliteal fascia, giving the impression that it would soon rupture through the skin. There was a great deal of pain, and impaired sensation and motion in the leg below the knee.

The large aneurysm sac was removed, and when this was completed there was a gap of about $3\frac{1}{4}$ in. between the ends of the popliteal artery. The proximal segment of the artery was found to be dilated to $\frac{5}{8}$ in. in diameter. The walls were thick and there was evidence of advanced calcareous degeneration. The distal segment was more normal in appearance and not dilated. The external jugular vein on the right side was removed. One was disappointed in this specimen, as there were multiple tributaries to the vein which made its size and shape irregular. The smaller end of this graft was less than $\frac{1}{4}$ in. in diameter, and the larger end when fully dilated was slightly less than $\frac{3}{8}$ in. in diameter. This venous graft was anastomosed to the segments of the artery, filling in the gap. There was such a great disparity in size and shape between the artery and venous graft that it was necessary to stretch the graft very greatly to complete the anastomosis. We had some fear that the overstretching of this segment of the vein would devitalize the wall and weaken it. With the anastomosis completed, the graft stretched across the cavity in the popliteal space with no living tissues to lie against the deeper surface. On the superficial aspect, the hamstring muscles and popliteal fascia were closed, which gave support and a source of blood-supply. Heparin solution was injected into the proximal segment of the artery so that it flowed across the suture

lines and through the graft. The clip was removed from the proximal segment of the artery and the circulation restored. Immediately there was distinct and forcible pulsation in the dorsalis pedis and posterior tibial arteries at the ankle. The patient was given heparin intravenously continuously for two weeks. The clotting time was maintained at a level between fifteen and eighteen minutes during this time. Following the operation the circulation to the foot was normal. The pain disappeared and motion in the foot was improved. (*Fig.* 430.)

For two and a half weeks following the operation the circulation remained normal in the foot. At this time the patient rather suddenly experienced pain in the popliteal space. While pulsations in the arteries of the foot were still good, they were less forcible than formerly. It was obvious on examination of the popliteal space that there was another aneurysm. Ten days following this, the popliteal space was again explored and the walls of a false aneurysm removed. The venous graft and segments of the artery including the anastomoses were dissected out. They were intact and appeared to be in excellent condition, with palpable pulsation in the graft and in the distal segment of the artery. Within $\frac{1}{4}$ in. of the proximal suture line, however, the anterior wall of the venous graft had bulged, forming a small aneurysm about the size of an acorn. One area of this aneurysm about $\frac{1}{16}$ in. in diameter had given way, and through this the interior of the vessel communicated with the false aneurysm in the popliteal space. This small opening was closed with a clip and the tourniquet removed. The circulation returned immediately and normal pulsation was visible and palpable in the graft and in the segments of the artery. With an arterial clamp on the proximal segment of the artery a probe was passed through the small opening in the aneurysm, demonstrating that both suture lines and the graft were patent. The wall of the graft was considerably thicker than when it was introduced at the first operation and it appeared to be going through the changes which we had observed repeatedly to have taken place in the experimental venous grafts. From the condition found at this second operation, I was impressed that the giving way of the venous graft had occurred in a segment of this structure which was overstretched. If a larger vein had been used which would have more nearly matched the size of the artery, probably this second accident would not have happened. On another occasion, a larger vein such as the opposite popliteal, femoral, etc., would be used.

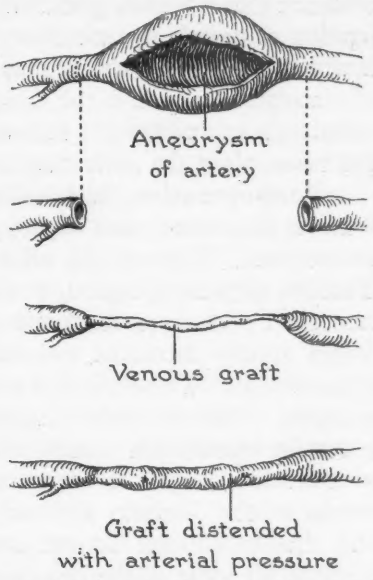

FIG. 430.—Use of venous graft for popliteal aneurysm.

The graft had such a healthy appearance that it was decided to repair the small aneurysm in its wall. Consequently the aneurysm was opened and a flap cut which could be sewn to the interior of the aneurysm to reconstruct a fairly normal lumen for this part of the vessel. The other wall of the sac was sutured over this to provide another supporting layer. When circulation was restored following this, the pulsation in the graft and distal segment of the artery were considerably

diminished, but it was easily demonstrated that there was an active blood-flow through these structures. Heparin was given into the proximal segment of the artery and the patient was heparinized for ten days following this. The circulation in the foot remained normal and the residual paresis improved fairly rapidly. Now, eight months after the operation, the patient is able to walk with only a slight toe-drop.

This case was most instructive as it demonstrated that a venous graft may survive in a human being and that such a graft could be kept patent by the use of heparin. While a small area of the wall of the graft failed, there were compensations, in that it provided the occasion for an exploration which demonstrated that, apart from this small area, the graft survived and functioned successfully. This provided evidence that a venous graft might be applied in many circumstances where formerly ligation of vessels was necessary. Even if the graft functioned for only a few days it would be useful. Under many conditions it would tide over an acute interruption of circulation, which is the dangerous period, and would allow time for a collateral circulation to develop. I believe, however, that if heparin is continued until healing has taken place the graft may continue to function indefinitely.

Post-operative Heparinization of Patients.—*Post-operative pulmonary embolism* is discovered with amazing frequency when post-operative deaths are carefully investigated. Due to the efforts of Belt,[47] in the Pathology Department of the Toronto General Hospital, a more careful study was carried out by developing an improved technique for performing the examinations. In the ensuing years he found greatly increased numbers of pulmonary embolisms in post-operative and other deaths. The clinical diagnoses in these cases were not more than 50 per cent accurate. This increase in death-rate from pulmonary embolism may be real to a certain extent, but almost certainly it is due to more accurate observation and post-mortem diagnoses on these cases. Belt found that more than 10 per cent of deaths at the Toronto General Hospital were the result of pulmonary embolism, and that in another 10 per cent there were pulmonary embolisms which might account for some of the clinical symptoms and be a factor in causing death.

With the experimental evidence that heparin would prevent thrombosis, it was decided to treat a large group of post-operative cases to see if heparin would affect the incidence of pulmonary embolism. Because of lack of sufficient funds this experiment had to be discontinued, but in the meantime about 400 cases have been treated. No thrombosis or embolism occurred in any of those cases which were free from it at the beginning of treatment, and in those in whom there was thrombosis there was no extension of this process. We intend to continue treating post-operative cases to obtain further information, as several thousand cases of this type will have to be treated before we can draw any definite conclusions.

The Time Heparin is Started in Post-operative Cases.—From experimental[48] and clinical experience, it has been proven fairly conclusively that heparin will not dissolve a blood-clot or a thrombus, either *in vivo* or *in vitro*. From this evidence it may be assumed that if the bleeding has been stopped at the time of operation, heparin will not start a hæmorrhage. To obtain hæmostasis, as in all good surgical technique, all the larger and medium-sized vessels should be tied off, or sealed with a cautery, and the small vessels will close spontaneously and will not be the source of a hæmatoma. It is possible, however, that vessels which do not bleed when the patient is in shock may bleed with a rising blood-pressure. If such a vessel is bleeding, heparin will allow it to bleed more than it would do otherwise.

For these reasons heparin is not administered for from 4 to 24 hours following operations, to allow the normal processes which control bleeding to operate. If there is any doubt about bleeding, the patient is not given heparin.

With the above-mentioned precautions, only 4 cases developed hæmatoma post-operatively while under the influence of heparin. The hæmorrhage stopped when heparin was discontinued, and all the patients recovered.

The Time Heparin is Discontinued.—The time thrombosis begins after operations is purely a matter of conjecture at present, but if stasis, changes in the composition of the blood, and eddying play a part, the patient under anæsthesia, with a lowered blood-pressure, in shock, and in cramped positions on the operating table or in bed, is under ideal conditions for the initiation of the process. The methods of combating these conditions, as described by many writers, do a great deal in decreasing the incidence of embolism, and it is hoped that the remaining difficulties may be overcome by the use of heparin.

The injection is discontinued when the patient has regained normal activity, i.e., when the factors thought to contribute to the production of thrombosis have ceased to act. This time has been reached when shock has passed and the blood-pressure and circulation are normal; the incision has healed and is not painful, so that deep respirations are possible; the patient feels well and energetic and moves about actively in bed and can exercise; distension is gone; the appetite has returned and the gastro-intestinal and urinary functions have returned to normal; the chest is clear; and the temperature and pulse are normal.

Selection of Cases.—It is hoped that the method of investigation used by Bancroft and his co-workers[49] will help in selecting those cases which are most likely to develop thrombosis. It is hoped that in these cases heparin, in appropriate amounts, may prevent the formation of a thrombus and thereby prevent embolism. Before starting treatment, the blood-clotting time, prothrombin index, platelet-count, bleeding time, and the other ordinary blood analyses must be ascertained.

Heparin for Laboratory Use, taking Blood Samples, etc.—Wilander[44] reported that sugar, calcium, uric acid, N.P.N., phosphatase, Hb, R.B.C., W.B.C., and hæmatocrit determinations are unaffected by heparinization. Heparin increases the resistance of erythrocytes to hypotonic salt solution, inhibits glycolysis, and alters the sedimentation rate. In addition all reactions involving complement may be affected because of the inhibiting action on complement mid-pieces. Plass and Rourke[45] found no change in the sedimentation rate of hæmophilic blood with and without heparin. Strom[46] asserts that heparin is unsatisfactory, the error in duplicate tests being much greater than with citrate.

Blood Transfusions.—Most of the earliest clinical experiments with heparin were in its use in blood transfusions. Since the purified heparin has been available we have used it fairly frequently with excellent results. There have been no deleterious results in our transfusions. Heparin was added to the blood, as it was drawn, in the proportion of one unit to each cubic centimetre in the ordinary transfusion of 500 c.c. The recipient would then receive 500 units, which is barely sufficient to change his clotting time. The other method which has been advocated is to heparinize the donor. The blood can then be drawn without danger of clotting and the dosage of heparin which the recipient would receive would be relatively small. This is an important point which must be considered if the patient is being transfused for hæmorrhage from a bleeding duodenal ulcer, for example.

If sufficient heparin were given to affect the clotting time of blood in the recipient it would encourage continued bleeding from the ulcer.

The cost of heparin required for transfusion has been mentioned as an objection to the method. With heparin at its present price, sufficient to give an ordinary transfusion by adding heparin to drawn blood could be procured for 35 cents (1s. 6½d.). The cost of citrate solution in ampoules provided by various drug houses is greater than that of this amount of heparin.

We propose to investigate the effects of heparin on lymph as a background for operations on patients who are suffering from lymphatic and venous obstructions. The interesting work of Widstrom and Wilander in preventing clotting of inflammatory pleural exudates suggests further possible uses of heparin in some of the lesions involving serous cavities.

SUMMARY

The discovery of heparin by Howell and the discovery of the purified barium salt by Best, Charles, and Scott have been discussed. Its chemical composition has been shown to be a mucoitin trisulphuric acid. This substance acts as an anticoagulant by intercepting the clotting process either as antithrombin or antiprothrombin.

A series of controlled experiments in animals have shown that the purified form of heparin is non-toxic. Other experiments on arteries and veins in animals have shown fairly conclusively that heparin will prevent thrombosis and clotting. Operations on blood-vessels may be carried out experimentally with greater success by using heparin. By continued injection of this substance, blood-vessels have been kept patent until healing has taken place. Venous grafts in arteries have been kept patent successfully, and have functioned satisfactorily for about one year.

Clinically, in over 400 patients in the wards of the hospital, heparin has been shown to have no toxic effects when reasonable doses are administered. In this group of cases there was no thrombosis of superficial or deep veins and in none of the cases did embolism occur. Cases with thrombophlebitis were thought to be improved by treatment with heparin. In a small group of cases with pulmonary embolism the effects of heparin were very striking. With one possible exception none of these cases had further embolisms and none of the patients died of pulmonary embolism. Operations on blood-vessels such as embolectomy were all successful when the vessels were cleared satisfactorily and treatment with heparin was carried out. In one case a venous graft was placed in an artery, and this remained patent and functioned satisfactorily. It is suggested that heparin is an important adjuvant in operations on blood-vessels where it is desired to keep the lumen patent. It may also be used to advantage in diseases where clotting and thrombosis of blood-vessels occurs.

CONCLUSIONS

1. Purified heparin is non-toxic in human beings and in experimental animals.
2. In diseases complicated by intravascular clotting heparin may be useful.
3. Experimentally heparin will prevent thrombosis and clotting in blood-vessels. Our clinical results thus far support these conclusions.

4. As these experiments are still in progress on both animals and human beings, final conclusions cannot as yet be drawn.

I wish to take this opportunity to acknowledge the assistance of Mr. L. B. Jaques, Dr. T. S. Perrett, Dr. R. Wilkinson, and Dr. R. MacKenzie. Financial assistance from the Banting Research Foundation in making grants at various times to these assistants is also gratefully acknowledged. Heparin used in earlier stages of this work was supplied without charge by the Connaught Laboratories. It gives me great pleasure to acknowledge the financial assistance of Mr. J. S. McLean in providing heparin for these experiments during the past year.

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SHORT NOTES OF RARE OR OBSCURE CASES

A CASE OF ACCIDENTAL AVULSION OF THE FORE-QUARTER WITH RECOVERY

By W. DRAKE LEE and FRANK RADCLIFFE
KETTERING AND DISTRICT GENERAL HOSPITAL

History.—D. N., aged 32, who was employed by Messrs. Stewarts & Lloyds, of Corby, Northamptonshire, was admitted to the Kettering and District General Hospital at 10.30 a.m. on March 26, 1938, with a complete avulsion of the right fore-quarter, and he was followed by an ambulance man bearing the limb complete with its clothing and wrapped up in some sacking.

On Admission.—The man was very shocked on admission, but as there did not appear to be any hæmorrhage through the dressing that had been applied, this was not disturbed and the man was treated for shock.

Figs. 431, 432.—Photographs of patient on discharge, showing the healing obtained.

The opportunity was taken to examine the avulsed limb, and it was found to consist of the arm complete with the scapula, but without the clavicle, and it appeared as if the greater part of the brachial artery and plexus would be found attached to the body.

At Operation.—At 2.30 p.m. the man had sufficiently recovered from shock to be taken to the theatre, and he was given open ether anæsthesia before any of the clothing was disturbed. When the clothing and dressings were removed a ragged hole in the skin was revealed and there was practically no hæmorrhage. The brachial

plexus was exposed in the wound, together with the twisted end of the brachial artery. The wound was cleaned up and the skin edges were excised, and the brachial plexus was crushed and ligatured as high as possible and the artery ligatured in two places. The outer half of the clavicle was sawn off, the skin edges were approximated with sutures, and two pieces of corrugated rubber drain were left in suitable positions.

PROGRESS.—The greater portion of the wound healed by first intention, but there was a discharge of pus from a portion of the wound for some considerable time; at no time, however, was there any cause for anxiety about the local or general condition of the patient, and in fact at no time was it considered necessary to resort to blood transfusion or intravenous saline.

The man was discharged from hospital quite fit on July 5, 1938, and the accompanying photographs were taken the day before his discharge (*Figs.* 431, 432).

Comment.—As the patient himself was unable to give an account of how the accident happened, the following report was obtained from his employers. At the time of the accident he was employed in the coal washing plant, and apparently his arm was caught in between the coal belt and a magnetic roller, but there were no witnesses of the accident, and it is assumed that he must have stumbled, and in attempting to save himself put out his arm, which was caught as stated.

In all probability this man owes his life to the fact that his arm must have been actually twisted out of his body, thereby sealing off the end of the brachial artery before any bleeding occurred from that source, and any hæmorrhage that did occur was probably only from the subcutaneous vessels.

We are indebted to Dr. D. Vincent Summers for the photographs.

SIMPLE NON-SPECIFIC ULCER OF THE ASCENDING COLON

BY THOMAS MOORE, MANCHESTER

WHEN one excludes ulcers of the colon due to colitis, dysentery, typhoid, tuberculosis, syphilis, stercal pressure, foreign bodies, and malignant disease, there remains a small group of simple non-specific ulcers. These, of unknown aetiology, are usually small and solitary. Although encountered in all parts of the large bowel they are most common in the cæcum and ascending colon. Since the lesion was first described in 1830 by Cruveilhier 60 cases have been reported. In 42 of these the ulcer was situated in the cæcum or ascending colon.

HISTORY.—A male, aged 35, was admitted to hospital on February 23, 1938. The previous morning, while putting on his right sock during dressing he felt a sharp pain in the right iliac fossa. This soon passed off, so that he took no notice of it and he carried on with his work as a shop assistant. Later in the day while walking up a steep hill, he experienced further sharp pains in the right iliac fossa which lasted for a few minutes. These discomforts were not sufficient to interfere with his normal routine and he retired to bed at the usual time and slept soundly. When he awakened on February 23 he felt perfectly well, but when raising the right leg to put on his sock the pain returned again in the right iliac fossa. This

time the pain persisted and he had to leave business about an hour before lunch because of it and a feeling of coldness. He had no pain in the back, and no nausea or vomiting. There were no urinary symptoms. The bowels had always been perfectly regular. He had always enjoyed good health and never had a previous illness.

On Examination.—The patient was in good general condition. The tongue was clean and the teeth in perfect order. Temperature 100·8° F. Pulse 90. *Abdomen*: There was definite tenderness in the right iliac fossa, which was maximum about ¾ in. below McBurney's point. There was slight muscle rigidity

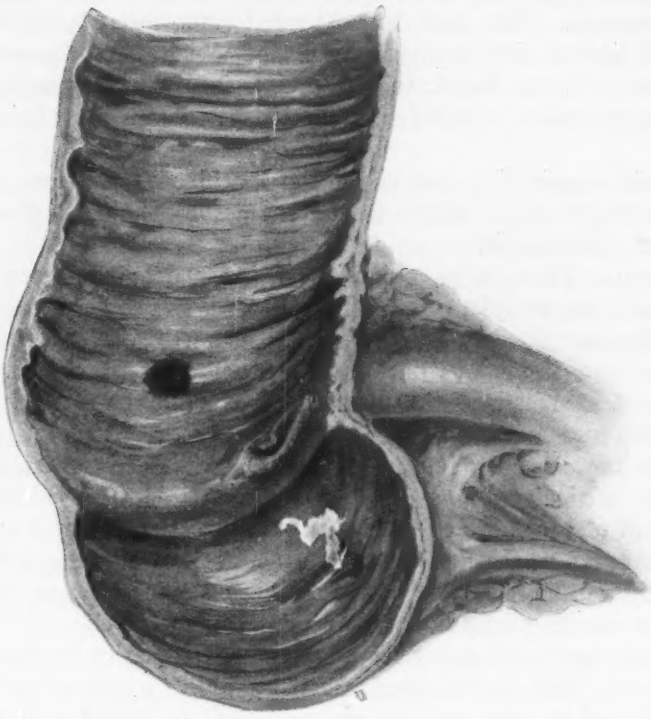

Fig. 433.—A portion of the specimen, showing the small ulcer in the lower part of the ascending colon.

in the right iliac fossa. No mass was palpable. The psoas test was positive and the obturator test was negative. No abnormality was detected on rectal examination. The cardiovascular, respiratory, and central nervous systems were normal on clinical examination. The urine contained no abnormality.

Pre-operative diagnosis: Acutely inflamed appendix lying on the psoas muscle.

At Operation.—At 11 p.m. the same evening, under spinal heavy percaine anæsthesia the abdomen was opened, using a McBurney incision. The appendix was subcæcal in position and was macroscopically normal. A mass about the size of a walnut could be felt in the posterior wall of the cæcum. There were some calcified lymph-glands in the mesentery of the terminal ileum and some enlarged glands behind the peritoneum medial to the ascending colon. The incision was extended upwards and laterally by simply cutting across the abdominal muscles.

The cæcum and ascending colon were mobilized, and excision of the right colon was performed. The ends of the terminal ileum and transverse colon were closed and lateral transverse ileocolostomy performed. The wound was carefully closed in layers. The patient had an entirely uninterrupted convalescence and was discharged on March 15, 1938.

THE SPECIMEN.—The specimen consisted of the last few inches of the terminal ileum, the cæcum, the ascending colon, and a few inches of the transverse colon. On opening the bowel on the lower part of the posterior wall of the ascending colon just above the level of the ileocæcal valve, a small punched-out ulcer about 3 mm. in diameter was seen (*Fig.* 433). Surrounding it there was a small circle of dark red mucosa. The ulcer had extended right through the bowel wall and communicated with a tiny cavity the walls of which were formed by thickened pericolic tissues. These, like those of the ulcer itself, were smooth, and there was no evident suppuration. Careful examination revealed no evidence of a foreign body.

Microscopic examination showed a non-specific inflammatory reaction in the colon surrounding the ulcer and in the fibrous tissue forming its floor. There was no evidence of tuberculosis.

Discussion.—There is no point in making a detailed survey of this lesion, as this was done very completely by Barron in 1928, and more recently by Cameron. A matter of constant interest, however, is the aetiology. The theories which have been suggested are legion, and include all possible causes of ulceration. From the punched-out character of the ulcer in this case, I have little doubt that the primary change is a vascular one, either thrombosis or spasm, which leads to necrosis of the bowel wall. Through the ulcer so formed infection occurs. This may give rise, particularly in anterior-wall ulcers, to local or diffuse peritonitis; in posterior-wall ulcers to an extending retroperitoneal cellulitis or local abscess; in other cases chronic perforation leads to a local inflammatory mass which may simulate a neoplasm, or the local peritoneal fibrous thickening in the region of the ulcer may give rise to partial obstruction of the large bowel.

Wilkie and later Cameron have suggested a similarity between these ulcers and peptic ulcers. Both lesions, they assert, occur near a part of the bowel guarded by a sphincter, where the contents are acid and the bowel wall has a relatively poor blood-supply. Wilkie has pointed out certain resemblances between the cæcum and the stomach. He believes that the medial wall of the former just above the ileocæcal valve corresponds to the lesser curvature of the stomach. In the four cases he reported, the ulcer usually occurred about this situation. Such views, though very ingenious, are pure speculation, and there is no real evidence to suggest any connection between the two conditions.

My thanks are due to Mr. H. H. Rayner, under whose care the patient was admitted to hospital, for permission to carry out the treatment of this case and make this report, and to Miss Davison for the coloured drawing.

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TOTAL RENAL INFARCTION

By Capt. F. A. B. SHEPPARD.
DISTRICT MEDICAL OFFICER, MADURA, S. INDIA.

The comparative rarity of this condition justifies the report of the following case :—

History.—K., an Indian servant, aged 24 years, was admitted to hospital on January 12, 1938, complaining of pain in the left loin. The onset, which was sudden and severe, had wakened him in the early hours of the morning three days before admission. The pain, though constant, had been slightly relieved by hot fomentations. He had vomited six times soon after the onset. Since the pain started, his appetite had been poor and the bowels were constipated. There was no frequency of micturition and the colour of the urine was normal. He had never passed any sand or stones, and had never noticed any blood in the urine. There was no history of any previous illnesses.

On Examination.—He was well nourished, and it was observed that he preferred to lie on the back with the left lower limb flexed. There was marked tenderness in the left hypochondrium and in the left costovertebral angle, and, while there was no real rigidity, the patient resisted attempts to palpate the left kidney. His spleen and liver were not palpable. The heart was normal in size and the sounds were clear and regular. The lungs were clear, and the nervous system was normal. The urine was normal on microscopical and macroscopical examination.

On January 13 a plain radiograph of the abdomen was taken and revealed nothing abnormal. The kidney shadows were normal in size and situation.

On January 17 an excretory pyelogram (uroselectan B) revealed a right kidney which was normal in size, shape, and function, but there was no excretion of the dye via the left kidney, which therefore appeared to be absolutely functionless.

During this period in hospital the pain in the loin continued, and was sufficiently severe to require morphia for its alleviation. The quantity of urine passed was within the bounds of normality and repeated examinations were clear. The temperature, which was 98·2° on admission, rose to 100° on January 14 and to 101° on January 17.

At Operation.—On January 19 the left kidney was exposed under spinal anæsthesia (10 c.c. of 1–1500 percaine), via the lumbar route. On delivery the organ was very slightly enlarged, soft, and flabby, and the constituents of the vascular pedicle were solid and matted together. There was no pulsation in the branches of the renal artery. The kidney was almost purple in colour, and on stripping the capsule oozed a little dark blood. Nephrectomy was performed, the vascular pedicle being secured by mass ligature. The cut ends of the vessels, both arteries and veins, were seen to be filled with clot. The wound was closed in the usual manner with a drain down to the pedicle. The kidney when split after removal showed no abnormality other than the previously noted congestion and flabbiness.

Following operation there was immediate relief of the pain, and the patient was discharged on February 7, 1938, after an uneventful and afebrile convalescence.

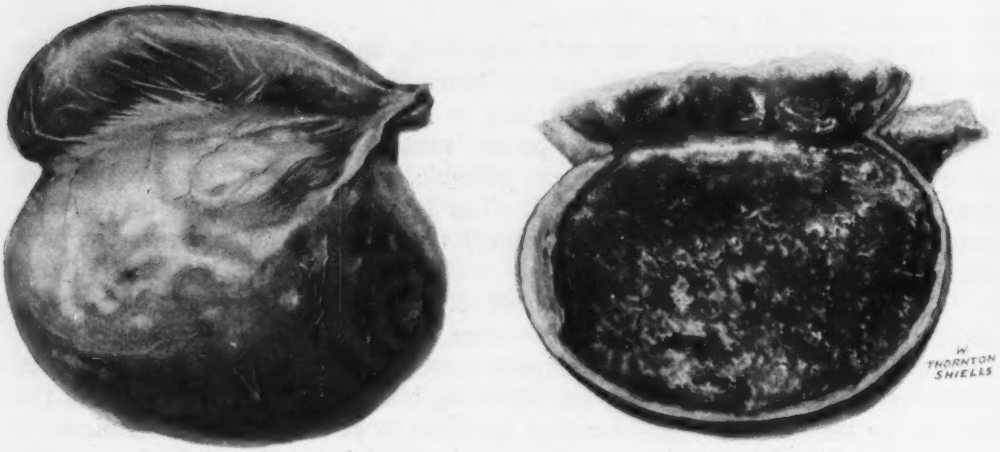
The particular case is of interest not only because of the rarity of the disease, but because of the complete absence clinically of any reason for its occurrence.

CALCIFIED HYDATID CYST OF THE LIVER

By MICHAEL J. SMYTH, London

When hydatid cysts of the liver die, they often become calcified. On X-ray examination the shadow cast by the cyst may prove puzzling unless the possibility of calcified hydatid is remembered. Intravenous injection of uroselectan or diotrast will help to distinguish it from renal calcification, but in the case illustrated here an ill-defined shadow was mistaken for the gall-bladder, and cholecystography did not help, as the cyst overlaid and obscured the gall-bladder.

History.—The patient was a thin little woman aged 62, who complained of flatulent dyspepsia and increasing discomfort in the right hypochondrium. She thought she could feel " something below the ribs."



A B

Fig. 434.—A, The cyst with the gall-bladder, to which it is firmly adherent; B, Section through the cyst.

On Examination.—A definite tumour, tender on pressure, was present in the region of the gall-bladder.

At Operation.—A tumour was found projecting from the anterior margin of the liver in front of the gall-bladder, which it had displaced backwards. The gall-bladder was firmly adherent to the tumour and it was not possible to dissect it free. The bile-ducts were exposed, the cystic duct and cystic artery ligatured and divided, and the tumour, together with the gall-bladder, was removed by wedge-shaped excision. Hæmorrhage was not severe and was easily controlled by mattress sutures of No. 2 catgut, which also served to bring the cut surfaces of the liver together.

The patient made a straightforward recovery.

The Specimen (*Fig.* 434).—On pathological examination the discovery of hooklets proved beyond doubt that the tumour was of hydatid origin.

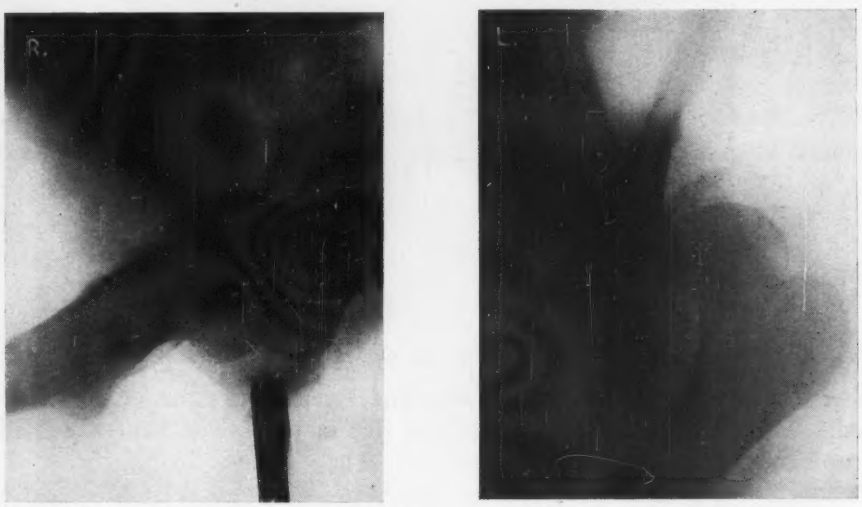
Comment.—It might be added that the patient had not lived abroad; in fact she had lived in London all her life, her greatest journey being a one day's excursion to Epping Forest on the outskirts of the city. The family did not keep a dog, nor was she in the habit of eating uncooked water-cress or lettuce.

A CASE OF BILATERAL TRAUMATIC DISLOCATION OF THE HIPS

By R. G. TAYLOR, Sheffield

In view of the fact that bilateral traumatic dislocation of the hips is a rare condition, less than 100 cases having been reported in the literature, the following account of a case, which was recently admitted to the Sheffield Royal Infirmary, may be of interest and worthy of note :—

History.—E. P., a male, aged 50, was admitted to the Sheffield Royal Infirmary, under Mr. F. W. Holdsworth, on October 17, 1938. He was sitting as a passenger in the front seat of a lorry, with both feet directed to the right, when a head-on collision occurred with another vehicle. This caused the front of the lorry to be driven in, with the result that his legs were pushed backwards and to the left, whilst his trunk was flung forwards and to the right.



A B

Fig. 435.—Radiographs showing: A, Right hip before reduction; B, Left hip before reduction.

On Admission.—He complained of severe pain in the left hip and in the back. He was very shocked. His temperature was subnormal and his pulse-rate rose rapidly to 130.

On Examination.—He was a big well-nourished man. His left leg was found to be flexed, adducted, and internally rotated. The head of the femur was palpable over the ala of the ileum. The greater trochanter was on a level with the left anterior superior iliac spine. His right leg was abducted, externally rotated, and flexed, and lay flat in this position on the surface of the bed. The head of the femur was palpable in the region of the obturator foramen on the under and inner aspect of the right thigh.

Radiological examination showed the following points :—

1. The head of the right femur was dislocated mainly downwards and slightly forwards. The bony acetabular rim was undamaged. (*Fig.* 435, A).

2. The head of the left femur was dislocated upwards and backwards. The upper and posterior rim of the acetabulum was fractured and driven upwards and backwards with the head of the femur (*Fig.* 435, B).

OPERATION.—Soon after admission, after the initial shock had passed off, both hips were reduced without difficulty under general anæsthesia. Reduction was confirmed radiologically (*Fig.* 436).

The tuberosity of the left tibia was transfixed by a Steinmann's pin. Skeletal traction was maintained by this means for three weeks. At the end of three weeks Unna's paste traction was applied, and the Steinmann's pin removed in order to prevent undue stretching of the knee ligaments. This traction was maintained for

FIG. 436.—Radiograph showing both hips after reduction.

a further five weeks. After the third week knee exercises for the left leg were commenced. The right leg was allowed to rest free in bed. The patient was allowed to sit up from the beginning.

PROGRESS.—The after-history of the case is as follows :—

January 10, 1939 : Still complains of pain in the left hip. Movements almost full in this joint.

January 31, 1939 : Left leg very swollen. Zinc-gelatin bandage applied to the leg below the knee, and a crêpe bandage to the knee.

February 21, 1939 : No change.

March 7, 1939 : Swelling much less. Still complains of pain.

March 28, 1939 : Considerable improvement. Less pain.

May 2, 1939 : Slight pain on flexion of left hip, otherwise full function.

Comments.—Dislocation of the hip is a relatively rare condition. For example, in a very large fracture department, during the last fifteen months, only 4 dislocations of the hip have been seen. Colonel A. M. Connell, who has had access to all the orthopædic cases at the Sheffield Royal Infirmary for the past forty-three years, informs me that he has never seen a case of bilateral traumatic dislocation of the hips. I have only been able to trace 62 cases in the literature. The first

appears to have been reported by Singowitz in 1830. All the possible combinations of this condition have been described, viz.: (1) Right anterior, left anterior; (2) Right posterior, left posterior; (3) Right posterior, left anterior; (4) Right anterior, left posterior.

The age incidence falls between 8 years and 72 years. The vast majority of these cases, as one would expect, were males. Posterior dislocations were found to be the least common.

The following complications were noted: (*a*) Inguinal hernia; (*b*) Hydrocele; (*c*) Paralysis of the common peroneal nerve. The average period of disability was 81 days. There were 8 failures, and the results of 4 cases were unknown; the remainder were successful results.

I am indebted to Mr. F. W. Holdsworth for permission to publish this case, to Dr. F. Kemp for the radiography, and to Colonel A. M. Connell for his helpful advice.

SUBCUTANEOUS EPIDERMOID CYSTS

By DOUGLAS MILLER, Sydney

The following subcutaneous cysts present unusual clinical and pathological features.

Case 1.—A male aged 51 had noticed a lump on the left side of his head which had been gradually increasing in size for about 18 months. When first noticed it was the size of a pea, but had increased very rapidly. No history of trauma.

Fig. 437.—*Case* 1. Low-power view of mural nodule. One of the cystic areas shows a tendency for a columnar type of cell in the wall.

On examination a spherical tumour 2·5 cm. in diameter was found situated beneath the skin of the scalp just above and behind the external auditory meatus.

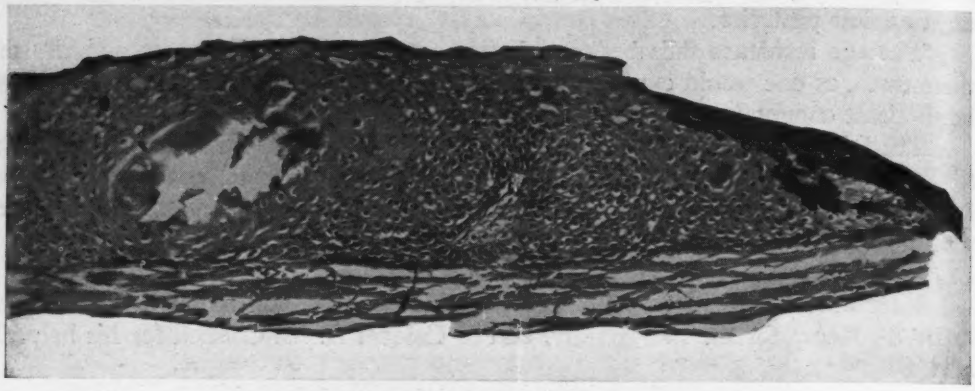


FIG. 438.—*Case* 1. Section of wall of cyst.

The skin was tightly stretched over it and was slightly telangiectatic. It was cystic, transilluminated brilliantly, showing a few opacities in its walls, and was unattached to underlying structures.

At operation the cyst was removed intact, the skin and deep fascia being readily separated from it.

Case 2.—A male aged 60 had noticed a lump on the dorsum of his forearm for a few years. It had gradually increased in size, and on one occasion had burst and discharged clear fluid. No history of trauma.

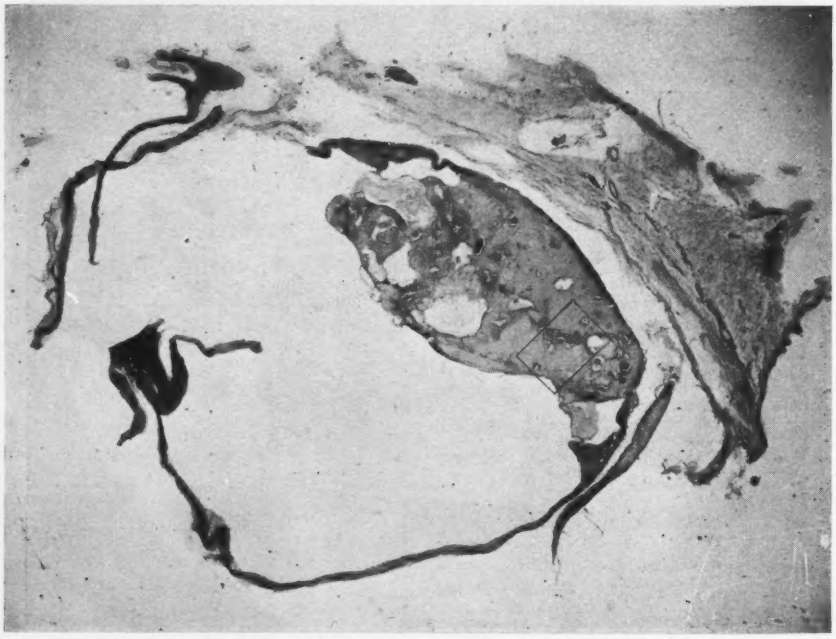


FIG. 439.—*Case* 2. Low-power view of mural nodule and part of cyst wall, showing multiple foci of cystic degeneration in mural plaque.

On examination a cystic tumour the size of a pigeon's egg was seen. It showed a brilliant transillumination, showing a few small opacities in its walls.

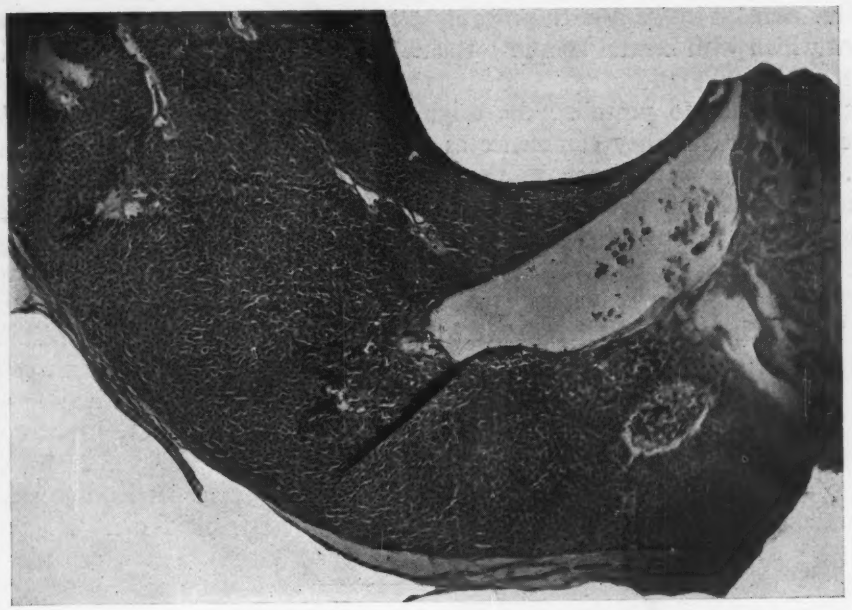


FIG. 440.—*Case* 2. Wall of cyst at junction with mural nodule, showing flattened epithelium lining large cyst. Small cystic space is also included.

It was situated in the superficial fascia, and the skin was slightly attached over its vertex.

PATHOLOGY

(*Figs.* 437–440.)

On dissection these tumours showed no tendency to invasion of the underlying structures and were readily separable from the skin. On naked-eye examination they appeared to be thin fibrous-walled cysts. They were filled by a clear yellowish serous fluid. On the inner aspects of the walls were several small white nodules, which on section were found to contain smaller cystic spaces.

Microscopically the cyst walls were found to be fairly completely lined by a thin layer of squamous epithelium which did not show papillæ. In parts the epithelium gave place to fibrous tissue. The mural nodules showed a structure of a curious epithelial type. Certain areas show a considerable degree of differentiation of cells with the elements of mature squamous epithelium recognizable, in inverted relations, the keratin being in the centre of the cell masses. These central areas of amorphous debris appear to be the starting points of the cystic spaces, which later enlarge into macroscopic proportions.

Other areas show much less differentiation, with solid masses of smaller cells with deeply staining nuclei. There is in these areas also a marked tendency to cyst formation, and in areas on the lining walls of these cysts there is a tendency for the cells to assume a column form suggestive of sudoriferous gland structure.

The watery nature of the cyst contents suggests that there is in fact a large sudoriferous element in this epithelium, the cystic spaces being fundamentally due to its proliferation and fluid production.

This element in the growth probably greatly overshadows the mature squamous element which with central keratin formation is microscopically such a conspicuous feature.

It is difficult to postulate the origin of these tumours, but the histological picture suggests that they commence as small solid nodules probably traumatic in origin. There is a tendency to the inverted type of growth of the epithelial elements, resulting in the formation of central cysts, which enlarge and coalesce, resulting ultimately in the preponderance of the cystic element and the relegation of the original nodule to the role of small mural plaques, situated in the wall of the cyst.

Though these cysts differ both in their contents and in their histological structure from the typical ' implantation cysts ', they possibly have some common causal factor. There is a largely undifferentiated element in the implant, from which the various epithelia differentiate along these several lines, probably with a primary tendency towards sudiferous types of epithelium, which later may undergo a metaplasia to the squamous keratin-forming type. It is suggested that they should be termed ' subcutaneous sudoriferous epidermoid cysts '.

LARGE PEDUNCULATED FIBROMA OF THE ŒSOPHAGUS

By L. E. GLYNN

FROM THE DEPARTMENT OF MORBID ANATOMY, UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL, LONDON

BENIGN tumours of the œsophagus are comparative rarities, only 62 cases having been recorded between 1717 and 1932 (Patterson, 1932). Of these the leiomyomata constitute by far the largest group, details of which have been summarized by Rose (1936). Very few reports of large pedunculated tumours are available, and often histological details are missing.

CASE REPORT

The patient was a woman aged 21, who complained of increasing dysphagia for four months. The onset was gradual and the general health good. No abnormality was found on examination of the neck or chest nor by indirect laryngoscopy.

A radiograph taken June 15, 1938 (*Fig.* 441) showed a dilatation of the upper thoracic part of the œsophagus, and delay in the passage of barium into the stomach. The dilated portion was not uniformly filled with barium, translucent areas being visible.

On June 21, 1938, a mobile polypoid tumour was seen by œsophagoscopy in the upper part of the thoracic œsophagus, apparently arising from the anterior wall, the posterior wall appearing normal throughout. Respiratory movements of the œsophagus were present at the tumour level, and there was no obstruction to the passage of the œsophagoscope at any point. Several pieces of the tumour were removed for biopsy. Following this operation there was an increase in the dysphagia, with considerable regurgitation of swallowed food, a deterioration of the general condition, and an elevation of the temperature.

A gastrostomy was therefore performed on July 6, 1938, under local anæsthesia. Two days later the patient complained of pain in the chest, accompanied by respiratory distress and inspiratory stridor. The following day there were signs of collapse at the base of the

left lung, associated with increased breathlessness and cyanosis: these symptoms were relieved by treatment in an oxygen tent. Oxygen therapy was continued until July 20, 1938, when the patient was well enough to leave the tent. For a while she continued to improve and became afebrile, but she had wasted considerably since admission and had become very weak. A cervical œsophagotomy was intended when the patient was sufficiently recovered, but she had a relapse about ten days after the cessation of oxygen therapy, with severe pain in the chest and profuse expectoration. She collapsed suddenly and died the following day (Aug. 7, 1938). During the interval of improvement she had been X-rayed again (*Fig.* 442). The large mediastinal shadow around which the barium was seen to flow, when it is compared with that of the previous radiograph, gives an indication of the extremely rapid growth-rate of the tumour.

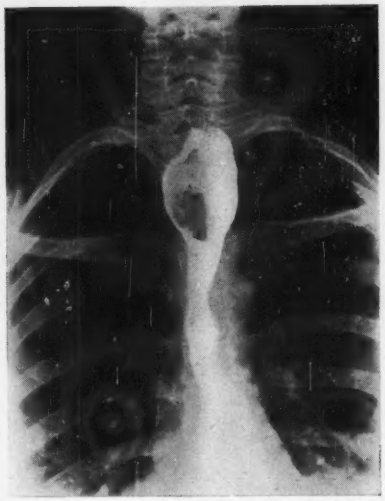


FIG. 441.—Radiograph of barium swallow taken June 15, 1938, showing œsophageal dilatation and areas of translucency due to a large pedunculated tumour. (× ⅛.)

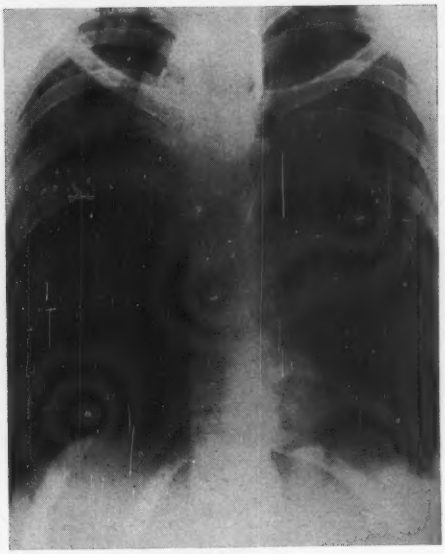


FIG. 442.—Radiograph of barium swallow taken Aug. 6, 1938, showing the considerable increase in the size of the tumour in seven weeks. (× ⅛.)

AUTOPSY FINDINGS.—Young adult female, moderately wasted. Healthy gastrostomy opening.

Heart: 300 g. Average size, myocardium pale and flabby.

Lungs: R. 800 g., L. 500 g. Heavier and firmer than normal. Fibrino-purulent pleurisy, with recent fibrinous adhesions between the left lower lobe and the diaphragm. Extensive bilateral confluent bronchopneumonia. Air-passages filled with brownish purulent fluid, not obviously compressed or distorted.

Liver: 1650 g. Slightly enlarged; very pale, cloudy swelling and some fatty change.

Spleen: 200 g. Recent fibrinous adhesions between spleen, stomach, and diaphragm.

Kidneys: 300 g. Congested; numerous petechiæ in both pelves.

Œsophagus: Arising from the midline anteriorly at about two inches below the cricoid cartilage was a large pedunculated tumour, 5 × 3 × 2 in., associated with a corresponding degree of œsophageal dilatation (*Fig.* 443). The peduncle was about ½ in. in diameter and ¾ in. in length. The œsophagus at the point of attachment was free from signs of inflammation or infiltration. The surface of the tumour, which showed a slight degree of lobulation, was necrotic and hæmorrhagic, and devoid of epithelial covering save over the stalk. Section showed the hæmorrhagic zone extending to a depth of about ½ in., the central mass being yellowish in colour and of gelatinous appearance and consistency. The neighbouring lymph-glands were slightly enlarged, but not infiltrated.

Stomach: Empty. Several fibrinous adhesions to spleen and diaphragm.

Peritoneum: Small subphrenic abscess between left dome of diaphragm and upper pole of spleen, containing about half an ounce of thick yellow pus.

HISTOLOGY OF THE TUMOUR.—Pieces of tissue were taken from the stalk, two places on the surface, and from the central gelatinous area. Sections from each were stained with Ehrlich's acid hæmatoxylin and eosin, Weigert's hæmatoxylin and van Gieson, Mallory's

FIG. 443.—Œsophagus and tumour photographed after fixation, which resulted in a considerable degree of shrinkage. The arrow indicates the point of attachment of the peduncle. (× ½.)

FIG. 444.—Central gelatinous area showing dense reticulum network of coarse and fine fibres. Laidlaw's reticulum stain. (× 340.)

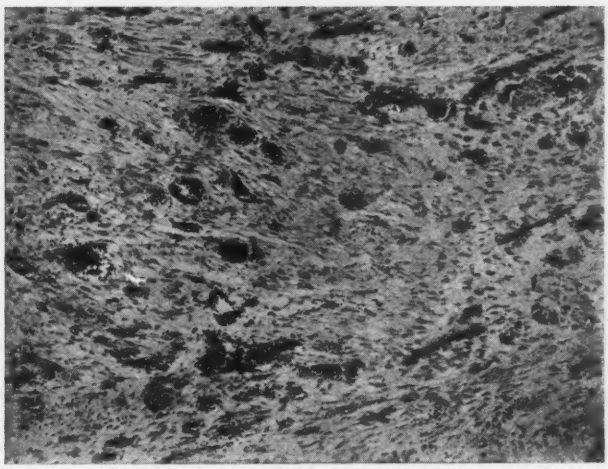


FIG. 445..—Tissue from anterior surface of tumour, composed of spindle cells and many thin-walled blood-vessels. H. & E. (× 72.)

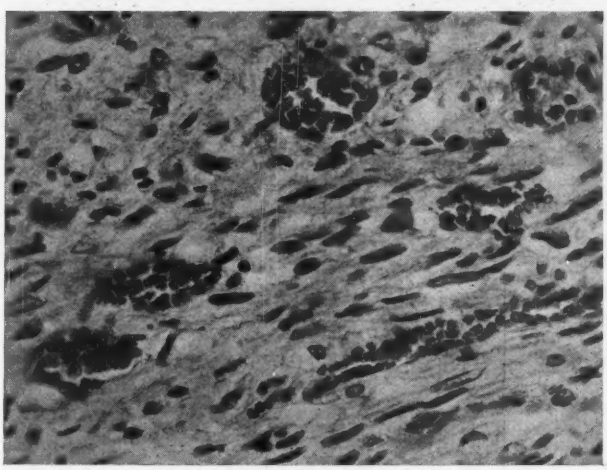


FIG. 446.—Same as *Fig.* 445, showing plump spindle cells, large thin-walled vessels, and absence of collagen fibres. H. &. E. (× 340.)

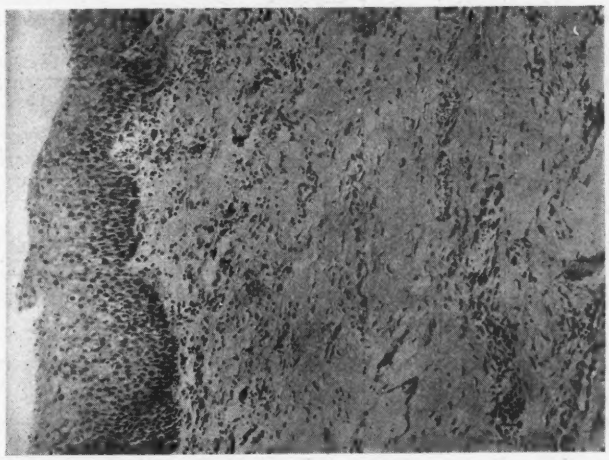


FIG. 447.—Part of peduncle, showing its stratified epithelial surface and its core of vascular areolar tissue. H. & E. (× 72.)

phosphotungstic acid hæmatoxylin, Laidlaw's reticulum stain, thionin and mucicarmine. The tissue from the central gelatinous area was composed of a network of coarse and fine reticulum fibres (*Fig.* 444). In the interstices of the latter were a number of well-formed blood-vessels, in each of which was a tangled meshwork of fibrin. Save for one small area of hæmorrhage and infiltration with polymorphonuclear cells, this part of the tumour was almost completely acellular.

The piece removed from the lower pole of the tumour was also rich in reticulum, but the bulk of the tissue was composed of collagen fibres with scanty fibroblasts uniformly distributed amongst them. A moderate number of well-formed blood-vessels were present, and in several areas there were collections of fibroblasts without accompanying collagen, but richly interspersed with fine argyrophil fibrils.

The biopsy material resembled closely the tissue from the anterior surface of the tumour, which was highly vascular and hæmorrhagic (*Figs.* 445, 446), the vessels being lined by only a single layer of endothelium. The intervascular tissue was composed of fibroblasts and reticulum fibres, but no collagen fibres. Despite the gelatinous appearance of the central mass of the tumour, specific staining for mucin was negative in sections from all the blocks.

With the exception of the pedicle, which consisted of areolar tissue covered by stratified epithelium (*Fig.* 447), the tumour was devoid of epithelial covering, presumably as a result of its extremely rapid growth and the friction to which it was exposed.

DISCUSSION

A study of the recent literature reveals 15 cases of benign pedunculated tumour of the œsophagus, the chief features of which are summarized in the table below. Of the 14 cases in which the sex is given, 10 were males and 4 females, and in 12 of the 15 cases the age incidence was over 40.

DETAILS OF 15 RECENT CASES OF BENIGN PEDUNCULATED TUMOUR OF THE ŒSOPHAGUS

AUTHOR	SEX	AGE	NATURE OF TUMOUR	SITE
Chitty, 1938	M.	26	Polyp	Posterior wall, upper end
Krieglstein, 1936	F.	42	Benign giant-celled tumour	Upper end near larynx
Kramer, 1934	M.	57	Fibrolipoma	Post-cricoid
Beutel, 1933	M.	50	Polyp	
Skold, 1933	M.	53	Lipoma	Posterior wall at level of diaphragm
Patterson, 1932	—	—	Myxofibroma	
Garretson and Hardie, 1928	M.	58	Fibrolipoma	Posterior wall, upper end
Dyke, 1927	F.	50	Polyp	Midline anteriorly at post-cricoid level.
Vinson, 1927	F.	54	Multiple polypi (inflammatory)	Middle third
Haenisch, 1924	F.	31	Fibroma	Midline anteriorly at post-cricoid level
Zehbe, 1924	M.	60	Fibroma	Upper end
Vinson, 1922	M.	62	Lipoma	Upper end
Breganzato, 1922	M.	50	Fibrolipoma	Upper end
Chaton, 1917	M.	74	Polyp	
Weigert, 1876	M.	54	Adenoma polyposum	Lower end

The point of origin in most instances was at the upper end of the œsophagus in the region of the cricoid cartilage. This has been taken to indicate an origin from congenital abnormality (Minski, 1895).

The diagnosis of fibroma in this case is based upon the fibrocellular composition of the tumour and the absence of muscle-fibres, fat, or myxomatous tissue. Of the 15 benign polypi referred to in the table only 2 are classified as fibromata (Haenisch, 1924; Zehbe, 1924) and in neither case is a detailed histological description available; 2 cases of lipoma, 3 of fibrolipomata, 5 polypi, 1 myxofibroma, 1 benign giant-celled tumour, and 1 adenoma constitute the remaining 13 cases.

One very unusual feature of the tumour here reported is its rapid increase in size as compared with its benign structure. This might possibly be due to œdema developing as a result of torsion of the pedicle, of which latter, however, there was no sign at the autopsy. On the other hand, the rapid increase in size may have been due to actual growth. The large number of reticulum fibres present, both absolutely and in proportion to adult collagen, was most striking. This comparatively immature state of the fibres in a connective-tissue tumour is possibly comparable to the apparently immature state of the cells in rapidly growing cellular neoplasms. This relationship between reticulum fibres and growth rate has been similarly commented upon by Foot and Day (1925). One is thereby tempted to correlate the rapidity of growth with the immaturity of the fibres, and to suggest the possible significance of the proportion of reticulum to collagen fibres in assessing the rate of growth of fibromata.

I wish to thank Professor R. S. Pilcher for permission to publish this case, and Professor G. R. Cameron for his kind assistance with the histological study of the tumour.

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REVIEWS AND NOTICES OF BOOKS

Fractures and other Bone and Joint Injuries. By R WATSON-JONES, B.Sc., M.Ch. Orth., F.R.C.S., Hon. Orthopædic Surgeon, Liverpool Royal Infirmary, and Robert Jones and Agnes Hunt Orthopædic Hospital. 9¾ × 7 in. Pp. 723 + xii, with 1040 illustrations, some coloured. 1939. Edinburgh: E. & S. Livingstone. 50s. net.

WE have received this book with a great sense of satisfaction, and after carefully reading it from cover to cover we have no hesitation in saying that it is the most important book on the subject which has appeared in recent years in the English language, and we are delighted to think that it is no longer necessary for English readers to turn to German text-books for the latest word on fractures. The first ten chapters deal with general principles of bone growth, injury, and repair and the complications which are liable to attend the healing of fractures. The most original chapter in this section is that on avascular bone necrosis. This is a subject which the author has made peculiarly his own by his observations and publication, and it is certainly one of which sufficient account has not been taken in the past. It affects particularly the healing of injuries in the neighbourhood of joints—the head of the femur, the head of the humerus, the astragalus, the carpal scaphoid, and the bony points about the elbow-joint. In considering the causes and treatment of delayed union and non-union a want of immobilization is regarded as the most important factor, whilst the interposition of soft parts between the bone ends is almost disregarded. We think that this is open to question because there are so many cases of non-union in which operative exposure reveals muscle or tendon interposed between the bone ends, notably in the middle of the shaft of the radius where the pronator radii teres is often found between the bone ends. In regard to the general principles of treatment a warning note is uttered about the dangers and disadvantages of skeletal traction. In particular the risks of a low-grade infection round the transfixing agent are emphasized. A very fair and reasonable attitude is taken about the operative treatment of fractures, intermediate between the extremes of the Lane school on the one hand and Böhler's treatment on the other. But it is evident that the author intends that the operative treatment of fractures should only be an exceptional resort, and for this reason there are not sufficient details given to enable the reader to take this as a guide to such operative procedures as, for example, the plating of fractures. The injuries of the wrist bones are given in very great detail, the fractures of the scaphoid being divided into three regional varieties, and we are glad to see that the early excision of part of the bone is admitted to be the best treatment under certain circumstances. As one would expect, the fractures of the neck of the femur are described in great detail, but the author is content with the main distinction between abduction and adduction fractures and he does not mention the classification of Paulweis, distinguishing the angle made by the line of fracture as a factor of great importance in treatment and prognosis. He lays down a very definite technique for the insertion of the Smith-Petersen nail and he commits himself definitely to the blind insertion under X-ray control.

It is impossible to review all the details of a book of this size and it would serve no useful purpose to criticize details in which the reviewer is at variance with the author. We can, however, say most sincerely that every part of the book is most instructive and stimulating. Perhaps the most important general reflection which comes to the mind on reading it is that it would have been impossible to have produced such a work except in a special department devoted to fracture work. In the preparation of the book there have been available the clinical and radiographic records of over 40,000 bone and joint injuries treated; most of these have been reviewed six or twelve months and sometimes five or ten years after the conclusion of the treatment. Certain subjects, such as the pathology of abnormal calcification and decalcification, of myositis ossificans, of spontaneous dislocation of the atlas, the treatment of fractures and dislocations of the spine, dislocations of the pelvis, and fractures of the neck of the femur, have already been the subject of monographs by the author both here

and in America. The book concludes with a section on rare injuries and unusual displacements, and a description of the organization and working of the fracture department of the Liverpool Royal Infirmary. One of the most commendable features is the list of references given at the bottom of almost every page to original articles in surgical literature. This is only one evidence of the enormous amount of work which has gone to the making of this treatise. There has perhaps been a tendency to include new methods because they are new, such as Roger Anderson's well-leg traction splint, whilst well-tried methods such as that of the Melbourne method of treating fractures of the femur are not mentioned. We could have wished that the book was not quite so large, and we think there is a good deal of extraneous matter, such as that dealing with pathological bone conditions, low backache, and rare cases, which might have been omitted, and we hope that in future editions the author will resist the temptation to enlarge the book still further.

In conclusion, we are delighted to offer our warmest congratulations to the author and his collaborators on their monumental work, which affords the finest possible tribute to those great men, Hugh Owen Thomas and Sir Robert Jones, who made Liverpool the very Mecca of orthopædic surgery and to whom the book is dedicated.

Treatment of War Wounds and Fractures, with Special Reference to the Closed Method as Used in the War in Spain. By J. TRUETA, M.D., late Director of the Department of Surgery, General Hospital of Catalunya, Barcelona. With a Foreword by ERNEST W. HEY GROVES, M.S., F.R.C.S., Emeritus Professor of Surgery, Bristol University. 7¼ × 5 in. Pp. 143 + xiii, with 48 illustrations. 1939. London: Hamish Hamilton Ltd. 8s. 6d. net.

THIS little book has appeared at a most opportune moment, for it contains the experience gained in a war just over and given to the world at the moment when another war is beginning. It is interesting to recall, as is done in the foreword, how the closed treatment of fractures was evolved from the experiences of the Great War. When Winnett Orr first proposed to treat septic bone conditions by encasement in plaster-of-Paris, his suggestions were met with incredulity and opposition. But when he demonstrated his method in this country the success which followed it converted the most sceptical. And now the problem of open fractures of bones has had to be faced on a very large scale. In the Spanish War this method of closed treatment by no means held the field at first, and it was only the stern teaching of necessity which brought it into general use. There are two points in the essential treatment of war wounds which are universally agreed upon: one is the necessity for excision of the skin edges and removal of all damaged tissue; and the second is the avoidance of constant changing of dressings. The third point upon which Dr. Trueta insists has not yet gained universal acceptance. It is the covering in of the whole wounded surface by plaster-of-Paris. The reason for this is the necessity for complete immobilization of the wounded tissues. The making of windows in the plaster opposite to the wound is fraught with the great danger of fresh infection and œdema, with bulging of the tissues through the window. The most serious criticism that has been made against the closed method is that it is liable to lead to gas gangrene. The large experience which Dr. Trueta has had, and the still larger experience of his colleagues, shows that this fear is unfounded. Gas gangrene will not occur if a timely and complete excision has been done, provided only that the main blood-supply of the limb is intact.

This little book deals more particularly with injuries of the bones and joints, and although the illustrations are often somewhat rough and ready they serve to make clear the chief points. Simplicity is one of the keynotes of the methods used and the very minimum of apparatus is necessary.

The Abdominal Injuries of Warfare. By GORDON GORDON-TAYLOR, O.B.E., M.A. (Aberd.), F.R.C.S., F.R.A.C.S. (Hon.), Senior Surgeon and Lecturer in Surgery, Middlesex Hospital, London. 9 × 6 in. Pp. 87 + viii, with 68 illustrations, some coloured. 1939. Bristol: John Wright & Sons Ltd. 10s. 6d. net.

THIS small book comes most opportunely at a time when we are preparing to deal once more with the wounds inflicted by warfare. In the main it is an illustrated account of the typical specimens of gunshot wounds of the abdominal organs found in the War Collection of the Royal

College of Surgeons. This war museum, beautifully preserved and catalogued, ought to be known and studied far more widely than it is. It would be well if Mr. Gordon-Taylor's example were followed by others, so as to give a complete account of the subject of war wounds. The book is beautifully illustrated by Mr. Thornton Shiells both in colour and in black and white.

But it is much more than a mere illustrated catalogue. The author gives a masterly summary of general principles and also of plain directions and advice in the conduct of abdominal injuries. He regards blood transfusion as the most important factor in securing success in desperate operations; he has no use for transfusion of saline or gum solution. The use of spinal anæsthesia is condemned in no uncertain terms. The account given of the successful treatment of multiple injuries shows the possibilities that surgery affords in the hands of a bold and resourceful surgeon.

Artificial Limbs and Their Relation to Amputations. $9\frac{5}{8} \times 6$ in. Pp. 88, with 42 illustrations (22 plates). 1939. London: H.M. Stationery Office. 3s. net.

THIS excellent work appears to be anonymous. His Majesty's Minister of Pensions in the Foreword states that it was initiated by Dr. Hebb and is based on notes of lectures by, *inter alia*, Dr. R. D. L. Kelham and Captain A. R. Maxwell. They will earn the gratitude of all who read it. The collective experience of those who have reviewed some 41,000 amputation cases, who oversee a service which supplies some 4000 prostheses annually, is clearly authoritative and almost beyond appeal. The calm and unbiased opinions reflected in the deliberate statements of the book are inherently convincing. It is not too much to say that it is almost impertinent to amputate without previous reference to this master key. Much of the contents cover that little-known gap between the pure technique of amputation and the pure craftsmanship of limb making, a field of knowledge that the wise surgeon will be anxious to acquire. There is an interesting account of the evolution of the present-day artificial limb. The rest of the book is devoted to the basic surgical and mechanical problems of limbs for the upper and lower extremities. The indexing is extremely clear and useful. The tragical timely appearance of such a work needs little emphasis.

Rectal Surgery. A Practical Guide to the Modern Surgical Treatment of Rectal Diseases. By W. ERNEST MILES, T.D., F.R.C.S. Eng., Senior Surgeon to the Gordon Hospital for Cancer, Fistula, and other Diseases of the Rectum. $8 \times 5\frac{1}{2}$ in. Pp. 359 + xi, with 2 colour plates and 105 illustrations. 1939. London: Cassell & Co. Ltd. 17s. 6d. net.

THE numerous friends and colleagues of Mr. Ernest Miles will welcome the appearance of this book as evidence of his perennial youth and activity. In it they will see, as would be expected from so precise and dogmatic a teacher, a full account of all those aspects of rectal work for which Miles is so well known, such as the anatomical arrangement of the primary and secondary hæmorrhoids and their three stages of development, the pecten band, recto-sigmoidectomy for procidentia, and abdomino-perineal excision for cancer of the rectum. The book is admittedly written entirely from a personal standpoint: there are very few references, and it would appear that much important contemporary work in this country, America, and elsewhere is ignored.

We do not agree with the statement on page 238 that the operability rate in this country is from 25 to 30 per cent. This is certainly a gross understatement of the present practice and merely points to the past.

It is natural to find the author heavily biased in favour of abdomino-perineal excision, and thanks to his pertinacity and long advocation of this operation it is generally recognized that there are many excellent reasons for a combined excision for eradicating a large proportion of rectal cancers. We see once again a record of the author's depressing experiences with perineal excision; his recorded operations, however, were done long ago (more than thirty years), and although in a small series of cases he had a recurrence rate of over 90 per cent this does not seem a sufficient reason for still condemning a method which has a considerable field of usefulness. The modern perineal excision will give at least 30 to 40 per cent of 5-year survivals, as many recent statistics have shown. Mr. Miles does take the trouble, in spite of his innate dislike of the operation, to describe a method of perineal excision in which the rectum is mobilized and removed from above downwards. This

seems to be identical with the method known as Goetze's operation, which is extensively practised on the Continent.

As regards end-results we are merely given (*a*) the same table of recurrence rates arranged according to four types of growth which was presented by the author before the Royal Society of Medicine in 1931, and (*b*) a 5-year survival rate figure produced by Mr. Lawrence Abel in October, 1935, from Cancer Hospital cases operated upon in the period 1920–1929 inclusive. An excellent opportunity of reporting some up-to-date tables of 5-year or even 10-year survival rates has thus been neglected.

A long chapter of forty pages is devoted to the subject of fistula, and excellent practical advice is given on the general principles of operative technique and after-treatment. The importance of defining the main track and its relationship to the anal musculature is stressed.

There is an interesting chapter on ulceration of the anus and rectum; evidently Mr. Miles has vivid memories of infective ulceration which used to be such a common and serious complication after rectal operations. In the final chapter on stricture of the rectum the teaching is that extensive tubular strictures are generally caused by infective ulceration; there is no mention of lymphogranuloma or the importance of Frei's test, nor is there a mention of rectal strictures following irradiation of the cervix uteri.

In his preface the author admits to many omissions, and some of these are rather striking, such as the absence of any note about injections for hæmorrhoids, or the use of oil-soluble anæsthetics for the treatment of fissures.

These criticisms are necessary because it might be assumed, from the title of the book and the reputation of the author, that Mr. Miles has produced a text-book of rectal surgery which would be a general introduction and guide to this special branch of medicine. It must be admitted that this book falls short of this standard. Its merit lies in the fact that it gives a vivid and dogmatic presentation of Mr. Miles' personal opinions.

Anæsthesia: Narcosis; Local; Regional; Spinal. By A. M. DOGLIOTTI, M.D., Professor of Surgery, University of Modeno. Authorized English Translation by CARLO S. SCUDERI, M.S., M.D., F.A.C.S., Associate in Surgery, University of Illinois, College of Medicine. 10¼ × 7 in. Pp. 680 + xx, with 236 illustrations, some coloured. 1939. Chicago, Ill.: S. B. Debour. $7.50.

THIS outstanding work professes to be the first work entirely devoted to anæsthesia in the Italian language. We welcome it as being evidence of the raising of the art of anæsthesia to the level of a speciality instead of allowing it to be practised by any newly qualified resident—the system which usually obtains on the Continent. It is remarkable in the second place as having been written by a professor of surgery. It is a scientific work of a high order, giving a good historical introduction, a careful physiological discussion, and a well-arranged description of the various methods of inducing anæsthesia. It is pleasing to find in a foreign text-book a generous acknowledgment of the parts played by Thomas Beddoes and Humphrey Davy (1799) in the discovery in Bristol of the anæsthetic properties of nitrous oxide. The role of many other pioneers is described most vividly, including that of August Bier, who tried spinal anæsthesia on himself.

The bulk of the book is concerned with a detailed description of various methods of general, local, and spinal anæsthesia. This is clear and well balanced. The indication for and against the different methods are fairly considered. Morphia and scopolamine are considered the best forms of premedication, and the use of paraldehyde has a very brief mention. Epidural injections, their method and use, are very fully described, and the indications for their therapeutic employment given.

The book is well illustrated and excellently translated.

The Art of Anæsthesia. By PALUEL J. FLAGG, M.D. Sixth edition, revised. 9 × 6 in. Pp. 491 + xxii, with 161 illustrations. 1939. Philadelphia and London: J. B. Lippincott Co. 30s. net.

SEVEN years have elapsed since the previous edition of this book, and during this period many new anæsthetic drugs have been introduced and the field of usefulness of the older ones clarified. It is very disappointing, therefore, that the author, who is personally a master in his field, should have revised his book so haphazardly.

It is impossible to avoid the conclusion that revision has been careless. Accepted modern methods, instead of being incorporated in the text, are in many cases just included in a chapter at the end of the book, and referenced by footnotes. The student reading the book will be left to decide for himself what is gold and what dross.

The earlier chapters show a rigid grouping of the classic anæsthetic substances—ether, chloroform, and ethyl chloride—and these bear the stamp of the first edition. Little emphasis is placed on the fact that a modern major anæsthesia usually requires a grouping of numerous anæsthetic substances.

At least two different modes of anæsthesia are given as the ideal anæsthetic. In this country we are prepared to admit that the ideal anæsthetic substance has not yet been found.

Apart from apparent hasty revision, there are a number of downright errors. There is much of repetition of the text, and some repetition of illustrations.

In a book of some 480 pages only 10 pages of text are devoted to spinal anæsthesia, and in these one reads of injury to the spinal cord in lumbar puncture at the orthodox site.

The book is not without value to the skilled anæsthetist who can overlook mistakes and condone numerous errors for the sake of some material of interest; it cannot be recommended to others.

Nitrous-Oxide–Oxygen Anæsthesia. McKesson-Clement Viewpoint and Technique. By F. W. CLEMENT, M.D., Director of Anæsthesia at Flower Hospital, Toledo; etc. 9¼ × 6 in. Pp. 274, with 70 illustrations. 1939. London: Henry Kimpton. 18s. net.

THE book is virtually a monograph on the art of nitrous-oxide-oxygen anæsthesia as administered by the McKesson apparatus. The author is clearly an enthusiast for that apparatus and does not bother to discuss any other machine for its administration. This will, unfortunately, limit the appeal of the book in this country, as centres where the apparatus is routinely used must be few. However, anæsthetists possessing the McKesson machine can hardly fail to profit from and enjoy the book.

The first two sections are devoted to theories of anæsthesia, the physical and chemical properties of nitrous oxide, and a good deal of useful practical physiology on anoxæmia, cyanosis, the role of carbon dioxide, rebreathing, shock, and the like. Most of the statements are sound, though occasional loose writing has crept in, such as: "An increase in pulse-rate produces a rise in both pulse pressure and diastolic pressure, while a fall in pulse-rate lowers the blood-pressure under normal conditions" (p. 62). Most physiologists would take exception to both verbs in that sentence.

The rest of the book is devoted to special techniques, special operations, a section on dental anæsthesia and analgesia, and finally a technical survey of the development of the gas apparatus by McKesson himself.

Of especial interest is the author's contention that a time interval is necessary to obtain relaxation with nitrous-oxide–oxygen, a point which surgeons often overlook, assuming that when the patient has "gone under" he is as relaxed as possible with the nitrous-oxide agent. The need for continuous charting of pulse-rate and blood-pressure as the only reliable means of detecting insidious oxygen lack is convincingly argued, and could be more widely appreciated.

It is a pity that status lymphaticus is still included as a cause of sudden death, when the Medical Research Council's report denies its existence.

The author's style is happy, and this note may well conclude with his own phrase, "No anæsthetic is safer than the person who administers it".

Textbook of General Surgery. By WARREN H. COLE, M.D., F.A.C.S., Professor of Surgery, University of Illinois College of Medicine; and ROBERT ELMAN, M.D., Associate Professor of Surgery, Washington University School of Medicine, Saint Louis. Second edition. 9¼ × 6⅛ in. Pp. 1031 + xxviii, with 559 illustrations. 1939. New York and London: D. Appleton-Century Co. Inc. 40s. net.

SINCE the appearance of the first edition of this book, three years ago, significant progress has been made in the domains of general surgery. In the second edition recent advances have been included to replace what is obsolete, without an increase in the size of the book.

The indications and method of instituting sulphonamide therapy are included in this edition. The value of this therapy in the treatment of intractable *Bacillus coli* infections of

the urinary tract is, however, not mentioned. The indication for mandelic acid in the treatment of infections by *Bacillus proteus* is not discussed.

An important new paragraph relating to the prevention of hæmorrhage in cases of obstructive jaundice has been added. Prothrombin is deficient in these cases, and the absorption of fats and vitamin K from the intestinal tract appears to be defective. The prophylactic treatment of cases of obstructive jaundice by pre-operative administration of vitamin K and bile-salts, supplemented by intravenous glucose and transfusion, is emphasized. The use of vitamin D in this connexion is also described.

A short description of "mixed tumours" of the lung is given. These appear to arise from fœtal rests, and explain the difficulty in the classification of many pulmonary tumours.

The value of the Miller-Abbot tube in the treatment of intestinal obstruction is discussed.

The Callendar modification of the Gritti-Stokes amputation at the knee-joint is described, but does not appear to provide a stump which English artificial limb makers would welcome.

In the treatment of actinomycosis it is stated that, contrary to the general belief, a cure may be expected if the diagnosis is made early. As well as deep X-ray therapy and surgical excision, the oral administration of thymol (1 g. per day) and saturation of the wound packing with 10 per cent solution of thymol in olive oil is suggested. The use of sulphonamide is also advised in this condition.

Conservative treatment of acute pancreatitis is looked upon with favour. The treatment of varicose veins is admirably described, but there is no comment upon the use of monoethanolamine oleate (Ethamolin) for injections.

The authors have omitted descriptions of operative technique, except in the case of a few of the every-day operations. They state wisely that an inadequate and brief description of an operation might lead to the erroneous conclusion that certain procedures were simple, and might be performed with inadequate preparation on the part of the surgeon.

The second edition of this excellent text-book is even better than the first, and will be most useful, not only for the medical student, but also for the post-graduate.

Les Pièges de la Chirurgie en Diagnostic et Thérapeutique. Erreurs ou Fautes ou Faits présumés tels. Conditions et Limites de la Responsabilité. By Professor E. Forgue and Professor Aimes. 9½ × 6½ in. Pp. 510. 1939. Masson et Cie. Broché, Fr. 90; Cartonné toile, Fr. 120.

A surgeon of long experience reading this book will recognize a great many of the pitfalls described, but it will be too late for him to avoid them. In the hands of a young man it will be a terrifying list; it must seem well-nigh impossible for him to run his course without disaster, and if he read the legal proceedings quoted, his chosen career must appear to head straight for bankruptcy. If, nevertheless, it is too late for him to become a lawyer instead of a doctor, he may realize the paramount importance of joining a defence association forthwith, and that will be all to the good.

The author, Professor Forgue, is quite frank about the difficulties and disadvantages of publishing an account of the many mistakes surgeons may make, even though they exercise all "reasonable care and skill". He considers, however, that the association with him of a junior colleague will guard against drawbacks and ensure to the theme a proper pitch.

It would be unfair to maintain the note of fundamental disagreement with the writing of such books. Here is the book, and it enshrines a multitude of sound observations arranged on a regional system, and no one who reads a few pages at a time can fail to be reminded of some danger he could and should guard against—if he remember in time. It becomes obvious that the author has had a career characterized by meticulous clinical investigation, careful operative technique, austere consideration for his patients' interests, and strict observation of professional obligations to colleagues.

Manual of Urology. By R. M. Le Comte, M.D., F.A.C.S., Professor of Urology, Georgetown University Medical Department. Second edition. 9 × 6 in. Pp. 295 + v, with 55 illustrations. 1939. Baltimore: The Williams & Wilkins Co. (London: Baillière, Tindall, & Cox). 18s. net.

This book contains a large amount of accurate information in a surprisingly small compass. It has been largely rewritten in the present edition and certain chapters have been added. The author's intention has been to produce a work for students commencing the study of

urology. It is doubtful if he has entirely succeeded in this, for the subject is too large to be condensed into so small a volume and yet be in a form easily assimilated by a beginner. It is more likely to be chiefly used as a work for quick reference by students working for higher examinations, and also by those recently qualified, for whom it contains much sound advice on the investigation of patients suffering from disease of the genito-urinary system. Most urologists will not, however, agree with some statements—as, for example, that if indigo-carmine injected intravenously appears from a kidney within ten minutes it may be considered to be a normal one and the opposite organ can be safely removed. It is also remarkable in a modern book to find that the method of separating the urine of either kidney by an intravesical segregator is alluded to at all. The description of the effect of spinal injuries upon the bladder function is incomplete, since no distinction is drawn between injuries of the cord itself and those of the cauda equina. It is impossible to agree with the pronouncement that operation should be advised in the case of benign enlargement of the prostate when the residual urine is 30 c.c. or more.

Cancer Laringeo. Su Tratamiento quirurgico. By Dr. RICARDO H. BISI. 10½ × 7 in. Pp. 366, with 101 illustrations. 1938. Buenos Aires: El Ateneo.

AT a time when irradiation is playing so considerable a part in the treatment of hypopharyngeal and laryngeal growths, it is exceptional to come across a book that leaves it out altogether, or makes but scant reference to its use for recurrences. Perhaps one reason is to be found in the author's statement that "the histological structure is without importance for surgical treatment". It is true the assertion is a preliminary to the obvious remark that for surgical success the one point of importance is to remove all the primary, and all the glandular metastases; but in the ears of an audience almost deafened by reiterations of the importance of 'grading' for prognosis, disrespect for histology sounds like heresy.

A considerable part of the book is given over to illustrated descriptions of operative procedures for growths in all the sites in the pharyngo-laryngeal area. The drawings are in the style made familiar by Pauchet, but not quite up to his standard.

In the early pages there are some reproductions of tomographic studies of the larynx in health and disease, which, if not very good, at least show promise of considerable usefulness in the near future. A sign of the author's thoroughness may be indicated by a list of no less than seventy named biological tests for cancer, though clearly he does not set much store by them.

There is not much that is new in his account of the signs, symptoms, or pathology of the neoplasms of the various sites, but he does bring out the importance of involvement of the hyo-thyro-epiglottic space.

For bibliography the reader is referred to other authors. It is doubtful if Trotter's writings have found a place in the author's library. Like all the books from "El Ateneo", the volume is very well produced.

Clinica Quirurgica en las Hidatidosis Costal y Pleural. By PEDRO D. CURUTCHET, Buenos Aires. 8½ × 6 in. Pp. 182, with 39 illustrations. 1939. Buenos Aires: El Ateneo.

THIS study of the clinical aspects of hydatid cyst of the ribs and pleura was suggested to the author, not so much by the rarity of the condition, as by a feeling of regret that it is often diagnosed only at operation, or as he says, by a pathological-anatomist's investigation *in vivo*.

The outstanding diagnostic point is this: that wherever a cyst invades the thoracic wall, affects the ribs by displacement or pressure-atrophy, causes a local bone destruction, or appears as a visible swelling on the surface, its origin is extrapulmonary.

Secondary invasion of the pleura from a cyst in the lung substance, which is not very rare, is accompanied by a pneumothorax and generally by a pyopneumothorax. On the other hand a cyst arising in the pleura or wall incorporates the visceral pleura in its adventitia, and displaces, but does not penetrate, the lung. Even the interlobar pleura resists invasion very well.

A curious point about parietal cysts is that they are generally flaccid, and subject to great variations in size, so that at times the known swelling may disappear from sight and palpation for months at a time, reappearing with an onset of pain.

The book is a careful piece of clinical research, illustrated by good radiographs.

The Study of Anatomy. Written for the Medical Student. By S. E. WHITNALL, M.A., M.D., B.Ch. (Oxon.), M.R.C.S., L.R.C.P., F.R.S. (Canada), Professor of Anatomy in the University of Bristol. Fourth edition. $7\frac{1}{4} \times 4\frac{7}{8}$ in. Pp. 124 + viii. 1939. London: Edward Arnold & Co. 4s. 6d. net.

As an introduction to the study of anatomy this little book is admirable. It sets out to impress the student with the fact that human anatomy must be considered in relation to the living body and its functions as well as future clinical work. But it is much more than this, for it deals with the fundamental philosophy of medical education and preaches lofty ideals for thought and conduct. We sincerely wish that every student will read it and follow its teachings.

Pioneers in Acute Abdominal Surgery. By ZACHARY COPE, B.A., M.D., M.S. Lond., F.R.C.S. Eng., Surgeon to St. Mary's Hospital, Paddington; Senior Surgeon to the Bolingbroke Hospital, Wandsworth Common. $7\frac{3}{8} \times 4\frac{7}{8}$ in. Pp. 134 + xii, with 38 illustrations. 1939. London: Oxford University Press. 7s. 6d. net.

MR. ZACHARY COPE has elaborated the interesting Bolingbroke Lecture which he delivered in May, 1938, into this little volume on "Pioneers in Abdominal Surgery". The pioneers are not arranged either in order of time or priority, but of each an account is given, and of each Mr. Cope has been at pains to provide a portrait. The subjects in the order of the chapters are: Obstruction of the large intestine due to stricture; Volvulus; Intussusception; Internal strangulation of the bowel; Perforative peritonitis; and Ruptured ectopic gestation. There is a table of references, an index of names, and another of subjects. The book is well written and informative, and may be read with pleasure and profit.

Sidelights on the Life of a Wearside Surgeon, 1859-1938. By WILLIAM ROBINSON, M.D., M.S., F.R.C.S. Eng., Hon. D.Ch. Durham. $8\frac{1}{2} \times 5\frac{1}{2}$ in. Pp. 154. 1939. Gateshead-on-Tyne: Northumberland Press Ltd. 5s. net.

DR. ROBINSON has done well to publish these sidelights. They should stimulate every general practitioner who reads them, for they show how much can be done by an energetic and able man with a bent for surgery to raise the tone of work not only in a town but in a whole district. From a practice in the mining village of Stanhope, Co. Durham, he moved to Sunderland, where he soon built up a large practice and did much good work first as physician and later as surgeon to the Infirmary. He describes the advances made, often on his own initiative, from an Infirmary of pre-Listerian days to the present time. He tells also of the rise of the eye hospital, from small beginnings to the present well-housed and well-equipped ophthalmic institution. Being endowed with a sense of humour, he recounts many good stories of the characters he has met with amongst his colleagues and patients.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest for our readers.]

Blood Transfusion. By VICTOR HORSLEY RIDDELL, M.A., M.D. (Cantab.), F.R.C.S. (Eng.), Assistant Surgeon and Lecturer in Operative Surgery, St. George's Hospital, London; Assistant Surgeon, Royal Waterloo Hospital, London; Consultant British Red Cross Transfusion Service. $8\frac{1}{2} \times 5\frac{1}{2}$ in. Pp. 370 + xv, with 65 illustrations, some coloured. 1939. London: Oxford University Press. 21s. net.

Il Cancro dello Stomaco. By LUIGI DI NATALE, Milan. $9\frac{3}{4} \times 6\frac{3}{4}$ in. Pp. 275 + viii, with 99 illustrations and 14 coloured plates. 1939. Bologna: L. Cappelli. L. 60.

Illustrations of Surgical Treatment, Instruments and Appliances. By ERIC L. FARQUHARSON, M.D., F.R.C.S.E., Tutor in Clinical Surgery, Royal Infirmary of Edinburgh. With a Foreword by Sir JOHN FRASER, *M.C.*, M.D., Ch.M., F.R.C.S.E., Regius Professor of Clinical Surgery, University of Edinburgh. $9\frac{1}{2} \times 6$ in. Pp. 338 + xii, with 259 illustrations and 57 plates of collections of instruments. 1939. Edinburgh: E. & S. Livingstone. 20s. net.

War Wounds and Air Raid Casualties. Articles republished from *British Medical Journal*. $8\frac{1}{2} \times 5\frac{1}{2}$ in. Pp. 258 + x. Illustrations. 1939. London: H. K. Lewis & Co. 10s. 6d. net.

Diagnosis and Management of Diseases of the Biliary Tract. By R. FRANKLIN CARTER, B.S., M.D., F.A.C.S.; CARL H. GREENE, A.B., Ph.D., M.D., F.A.C.P.; and JOHN RUSSELL TWISS, A.B., M.D., F.A.C.P., New York Post-Graduate Medical School, Columbia University. 9¼ × 6 in. Pp. 432, with 84 illustrations and 6 plates. 1939. London: Baillière, Tindall & Cox. 32s. 6d. net.

Patologia y Cirugia del Espinter de Oddi. By DELFOR DEL VALLE, Professor Extraordinary of Clinical Surgery, Gastroenterological Institute of Hospital Ramos Mejía. 9 × 6¼ in. Pp. 275, with 55 illustrations. 1939. Buenos Aires: El Ateneo.

Irving's Anatomy Mnemonics. By ALASTAIR G. SMITH, L.R.C.P. and S. (Edin.), Senior Demonstrator in Anatomy, Surgeon's Hall, Edinburgh. 4¼ × 2⅝ in. Pp. 133. 1939. Edinburgh: E. & S. Livingstone. 1s. 6d. net. Fourth edition, revised and enlarged.

The Surgery of Injury and Plastic Repair. By SAMUEL FOMON, Ph.D., M.D., formerly Major Medical Corps, U.S. Army. 10 × 6¾ in. Pp. 1409 + ix, 925 illus., some coloured. 1939. Baltimore: Williams & Wilkins Co. (London: Baillière, Tindall & Cox.)

Illustrations of Bandaging and First Aid. By LOIS OAKES, S.R.N., D.N., Nursing Editor, *Nursing Illustrated*; Examiner to the General Nursing Council. 7¾ × 5¼ in. Pp. 248 + viii, with 290 illustrations. 1939. Edinburgh: E. & S. Livingstone. 6s. net.

Pathological Histology. By ROBERTSON F. OGILVIE, M.D., F.R.C.P. (Edin.), Lecturer in Pathology, University of Edinburgh; Senior Pathologist, Royal Infirmary, Edinburgh; etc. With a Foreword by Professor A. MURRAY DRENNAN. 8⅝ × 5½ in. Pp. 332 + x, with 220 photomicrographs in colour by T. C. DODDS, F.R.P.S., F.I.B.P., Senior Technician, Pathology Department, University of Edinburgh. 1939. Edinburgh: E. & S. Livingstone. 27s. 6d. net.

Tumours of the Hands and Feet. By GEORGE T. PACK, B.S., M.D., F.A.C.S., Assistant Clinical Professor of Surgery, Yale University School of Medicine, and Cornell University College of Medicine; Attending Surgeon, Memorial Hospital for Cancer and Allied Diseases. 10 × 6¾ in. Pp. 138, 64 illus. 1939. London: Henry Kimpton. 15s. net.

Hospital for the Ruptured and Crippled. A Historical Sketch written on the occasion of the Seventy-fifth Anniversary of the Hospital. By FENWICK BEEKMAN, M.D. With a Foreword by PHILIP D. WILSON, Surgeon-in-Chief. 9 × 6 in. Pp. 157, with Frontispiece and 10 Plates. 1939. Printed privately in New York (copies from Superintendent). $3.00.

Wide Field X-ray Treatment. The Value of the X-ray Bath Method in Disease and Health. By S. GILBERT SCOTT, M.R.C.S., L.R.C.P., F.F.R., D.M.R. & E. (Camb.), Consulting Radiologist to the London Hospital; Honorary Radiologist to the British Red Cross Rheumatism Clinic, London; Honorary Physician Radiologist to the Charterhouse Rheumatism Clinic. 8½ × 5½ in. Pp. 80 + xvi, with 13 illustrations. 1939. London: George Newnes Ltd. 8s. 6d. net.

A Text-book of X-ray Diagnosis. By British Authors. Edited by S. COCHRANE SHANKS, M.D., M.R.C.P., F.F.R., PETER KERLEY, M.D., M.R.C.P., F.F.R., D.M.R.E., and E. W. TWINING, M.R.C.S., M.R.C.P., F.F.R., D.M.R.E. In three volumes. 9¾ × 7¼ in. Vol. III, Skeletal and Nervous Systems. Pp. 800 + xiv, with 710 illustrations. 1939. London: H. K. Lewis & Co. 63s. net.

An Index of Treatment. By various writers. Edited by Sir ROBERT HUTCHISON, Bt., M.D., LL.D., P.R.C.P., Consulting Physician, London Hospital, and Hospital for Sick Children, Great Ormond Street; assisted by REGINALD HILTON, M.A., M.D., F.R.C.P., Physician to St. Thomas's Hospital; Consulting Physician, Radium Beam Therapy Research, Farnborough Hospital, Kent, and Wembley Hospital. Twelfth Edition, revised. 10¼ in. × 6½ in. Pp. 996 + xv, with 148 illustrations. 1940. Bristol: John Wright & Sons Ltd. 42s. net.

Demonstrations of Physical Signs in Clinical Surgery. By HAMILTON BAILEY, F.R.C.S. (Eng.), Surgeon, Royal Northern Hospital, London; Surgeon and Urologist, Essex County Council; Surgeon, Italian Hospital; Consulting Surgeon, Clacton Hospital and the County Hospital, Chatham; External Examiner in Surgery, University of Bristol. Seventh Edition, revised. 9 × 6 in. Pp. 310 + xii, with 377 illustrations, some of which are in colour. 1940. Bristol: John Wright & Sons Ltd. 21s. net.

A Synopsis of Surgery. By ERNEST W. HEY GROVES, M.S., M.D., B.Sc. (Lond.), F.R.C.S. (Eng.), Consulting Surgeon to the Bristol General and Municipal Hospitals, and to the Treloar Cripples' Hospital, Alton, Hants; etc. Eleventh edition. 7¼ × 4⅞ in. Pp. 714 + viii, with 195 illustrations and 13 coloured plates. 1940. Bristol: John Wright & Sons Ltd.